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Backhouse

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(54) **FLUIDIC DEVICES**

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(73) Assignee: **Micralyne Inc.**, Edmonton (CA)

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Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

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(51) **Int. Cl.**[7] **H02K 44/00**; F04F 11/00

(52) **U.S. Cl.** **417/92**; 417/50

(58) **Field of Search** 417/50, 92, 65, 417/48, 68, 322; 210/222, 223

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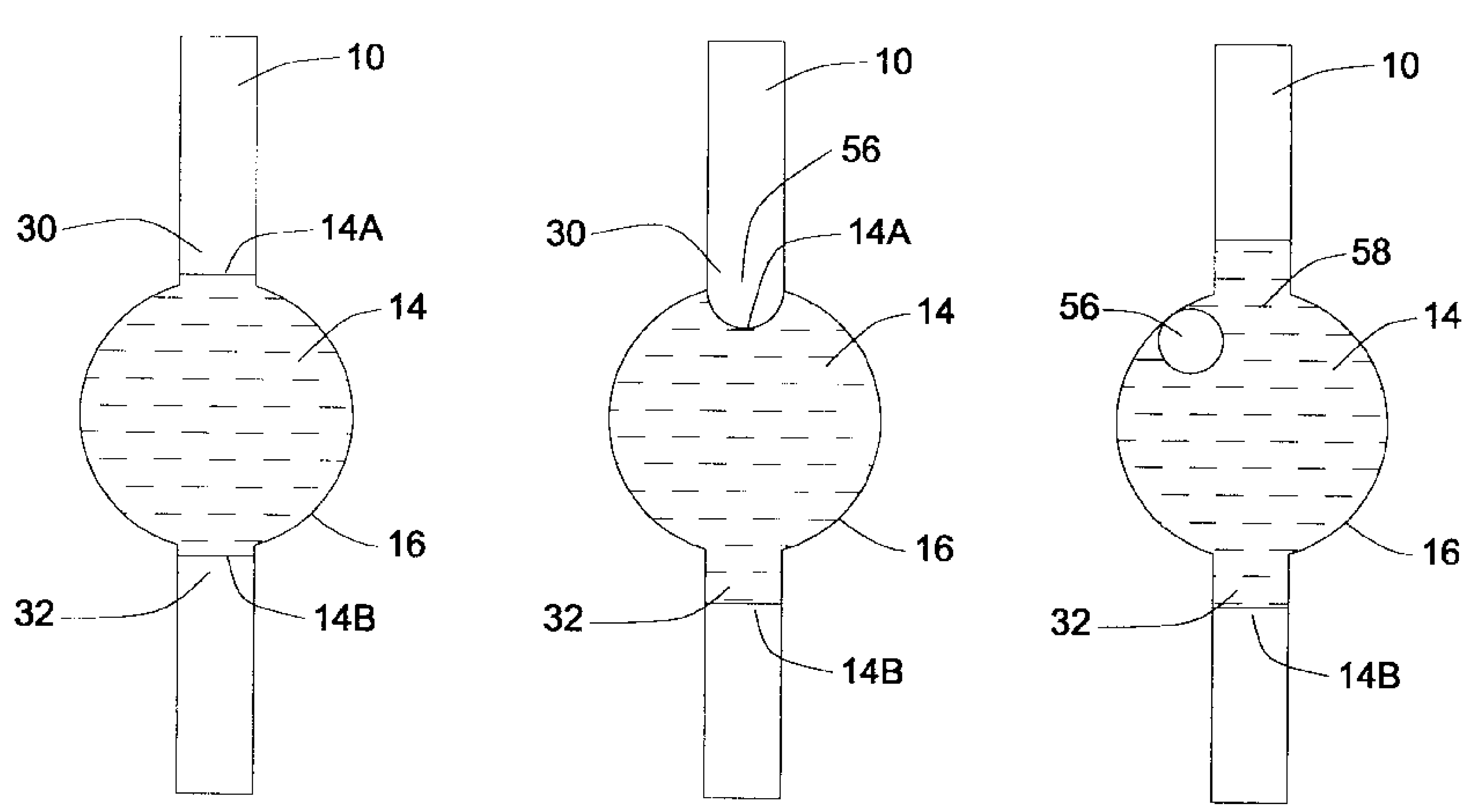
(57) **ABSTRACT**

A microfluidic device operates as a pump for pumping fluid along a channel in a microchip by moving a drive fluid in the channel under the influence of a force field that is generated externally to the channel. The drive fluid is preferably a ferrofluid, and the force field is preferably a variable magnetic field. Drive fluid, driven by variation of the magnetic field, drives driven fluid through the channel. The drive fluid is recirculated, in one case by rotating the drive fluid within an enlargement in the channel, and in another case by returning the drive fluid along a return channel. A valve is formed by using a ferrofluid plug as a movable barrier for fluids in a channel. The microfluid device may be formed between two plates forming a microchip. The channels may be as small as 1 μm to 100 μm. Methods of pumping fluids by using an in channel drive fluid and exterior drive are also disclosed.

6 Claims, 13 Drawing Sheets



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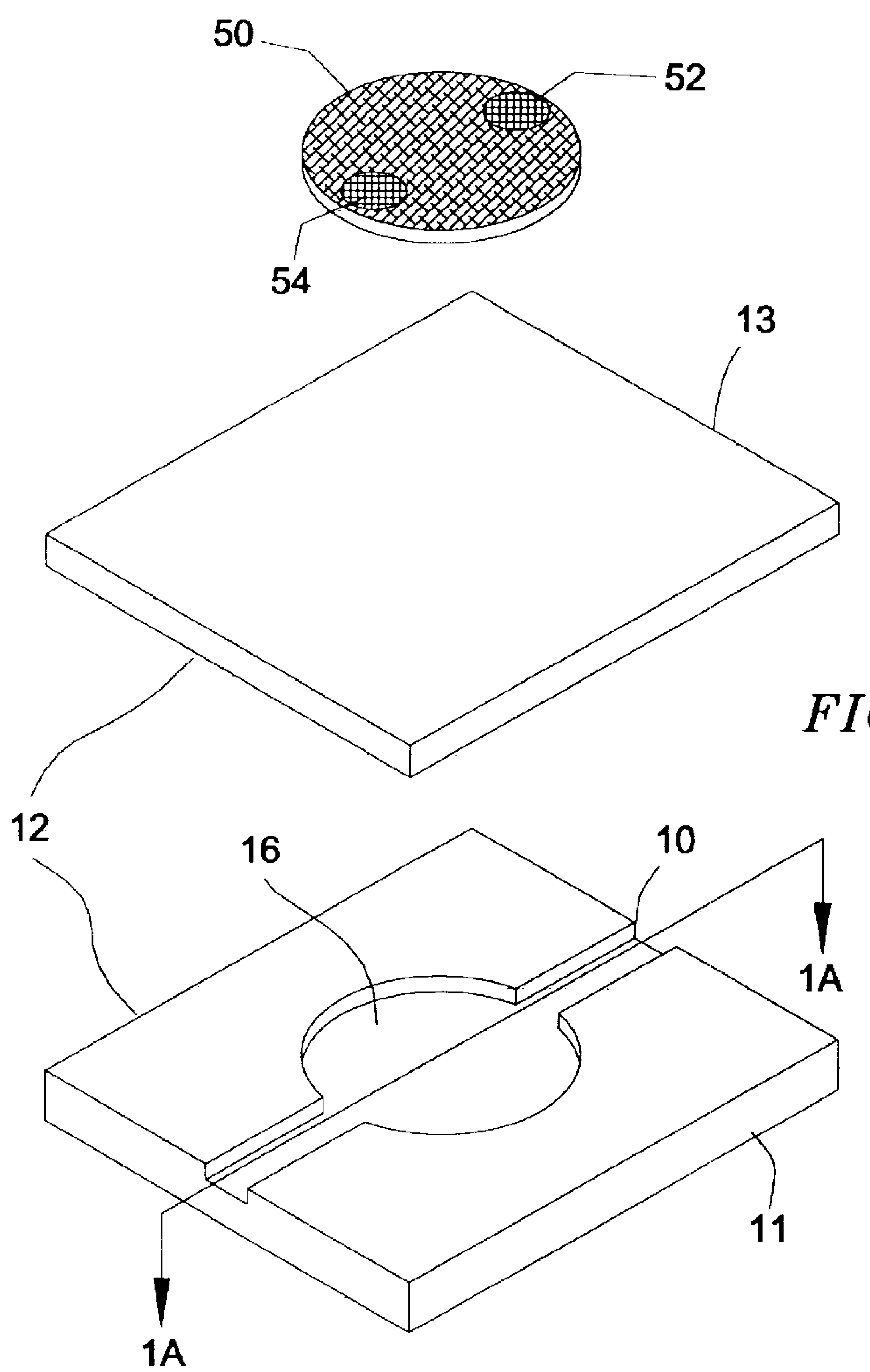
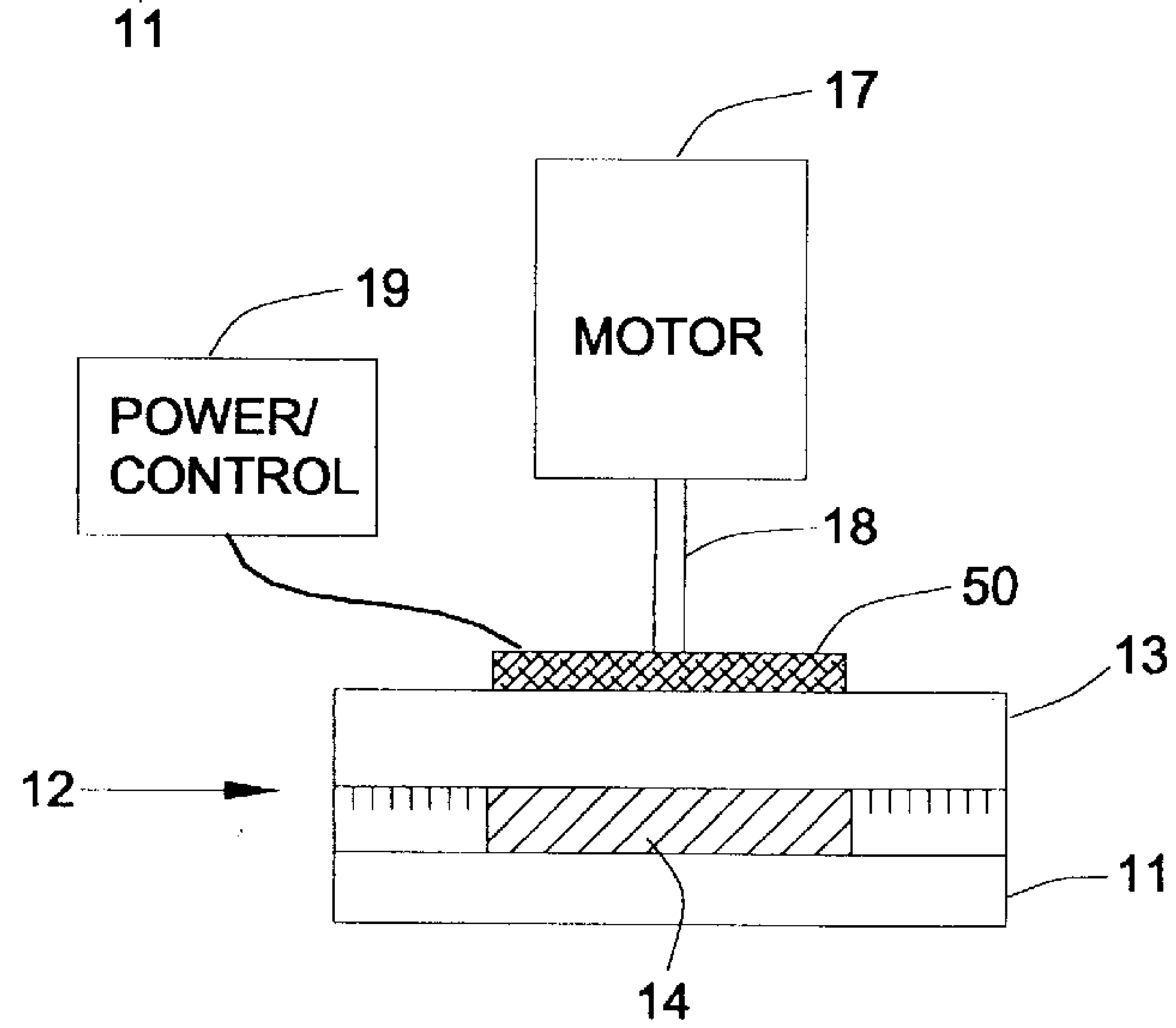

50
52
54
13
12
16
10
1A
11
1A

FIG. 1


17
MOTOR
19
POWER/
CONTROL
18
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13
12
11
14

FIG. 1A

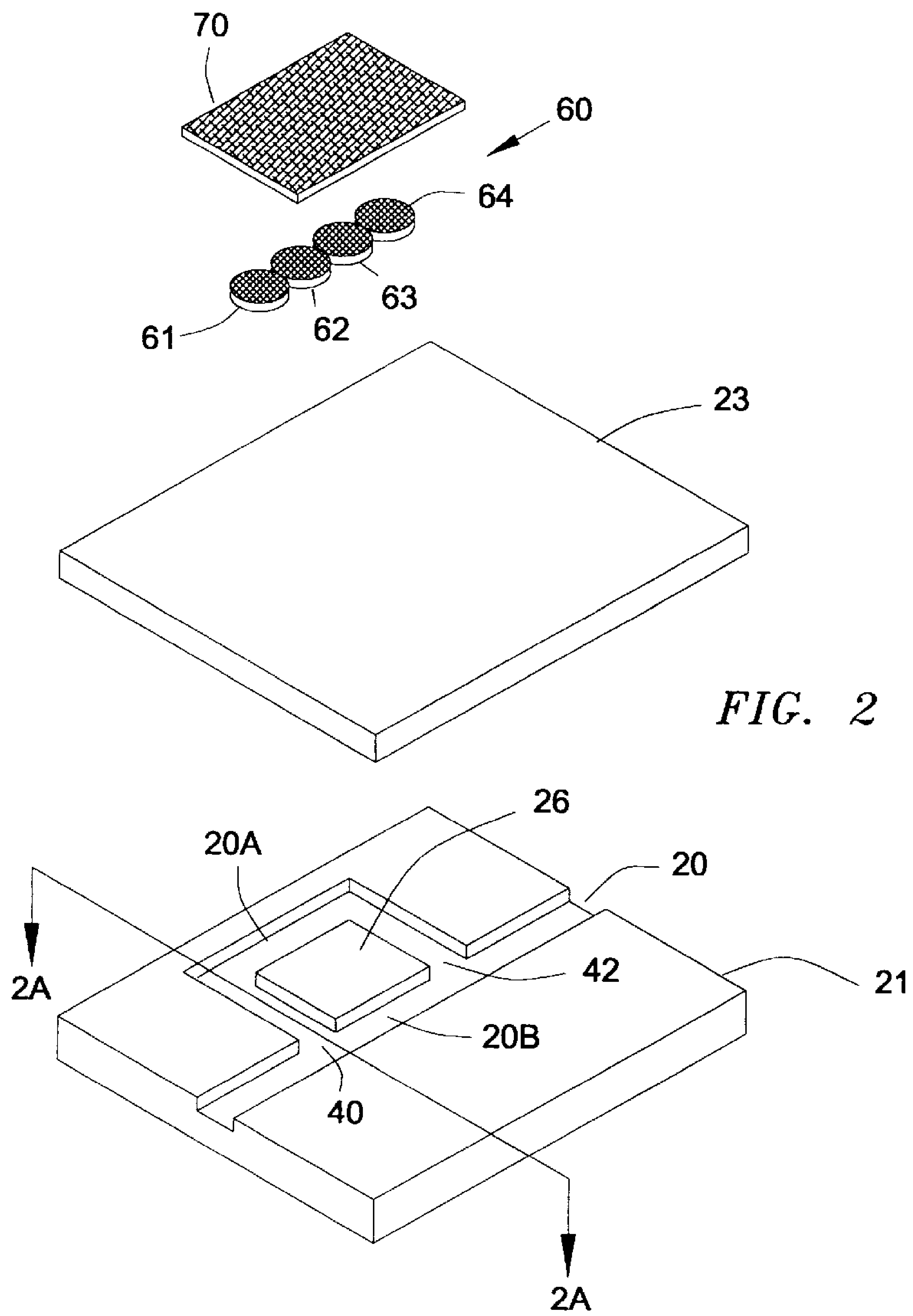


FIG. 2

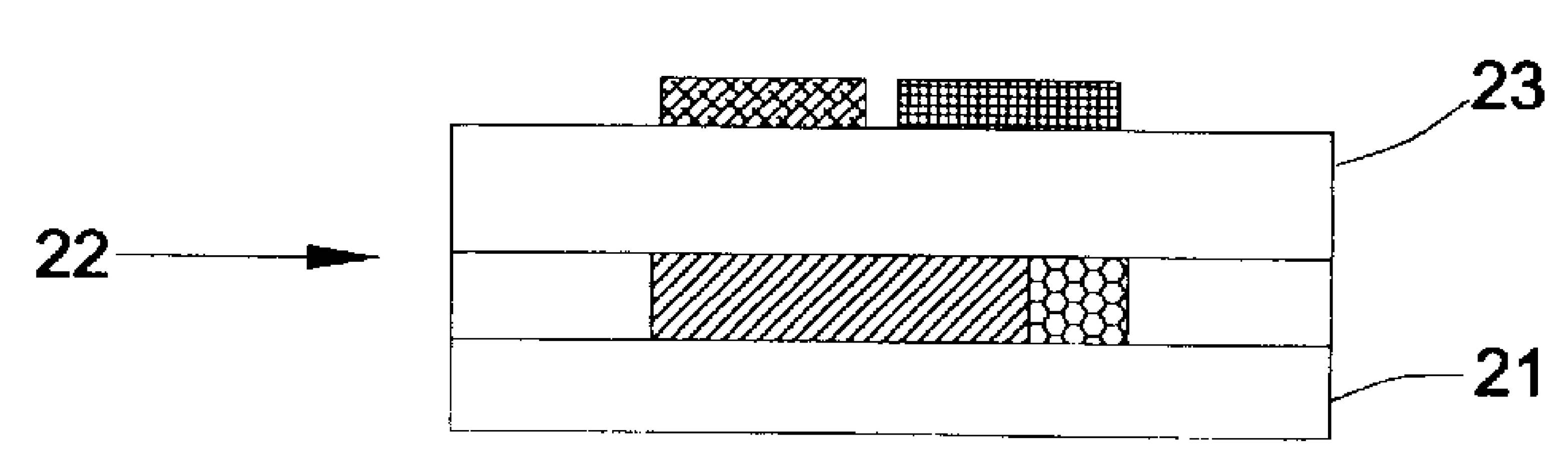


FIG. 2A

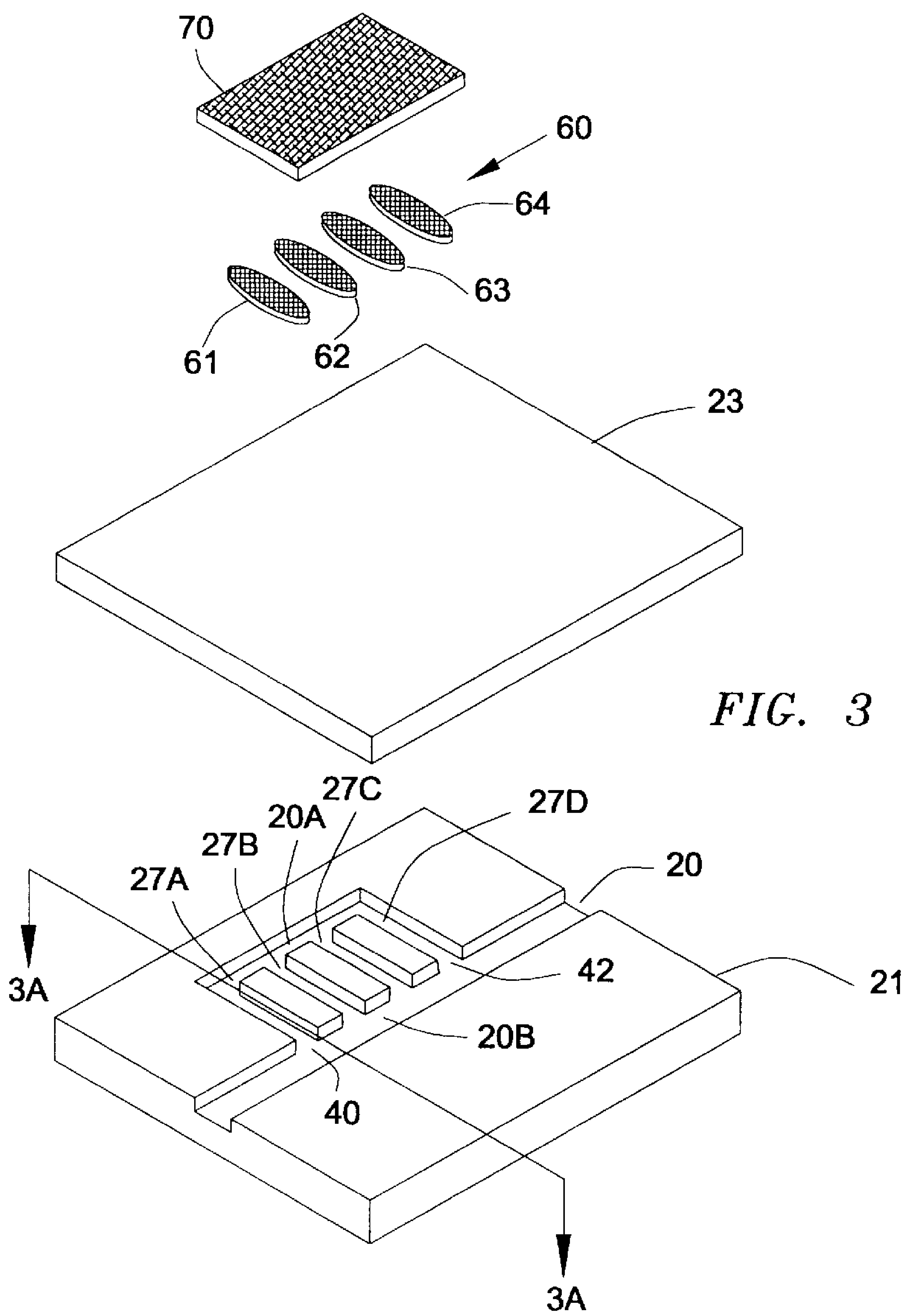

70
60
64
63
61
62
23
27C
27D
20A
27B
20
27A
3A
42
21
20B
40
3A

FIG. 3

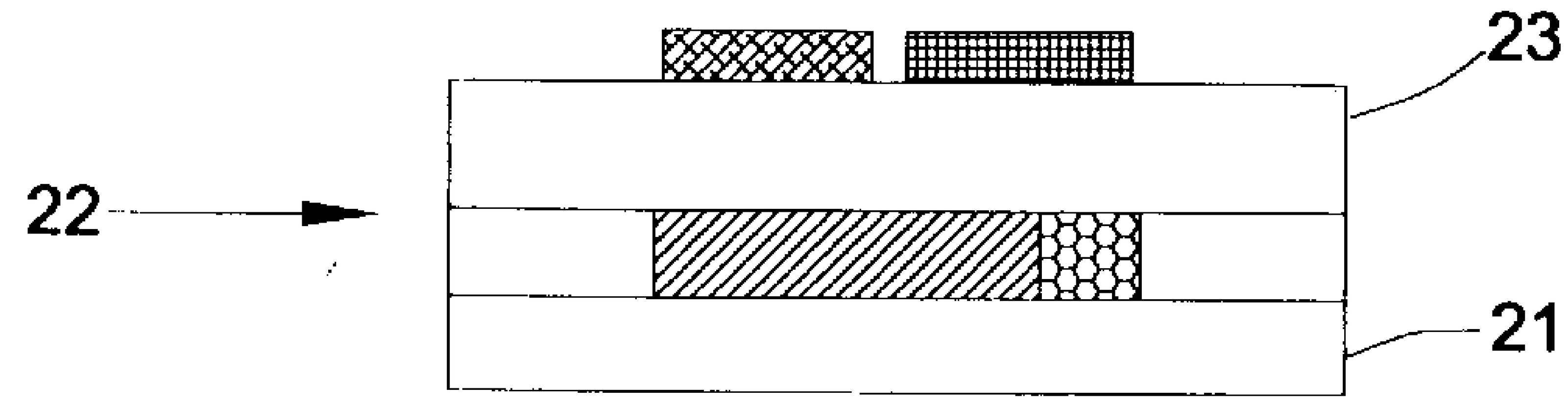

23
22
21

FIG. 3A

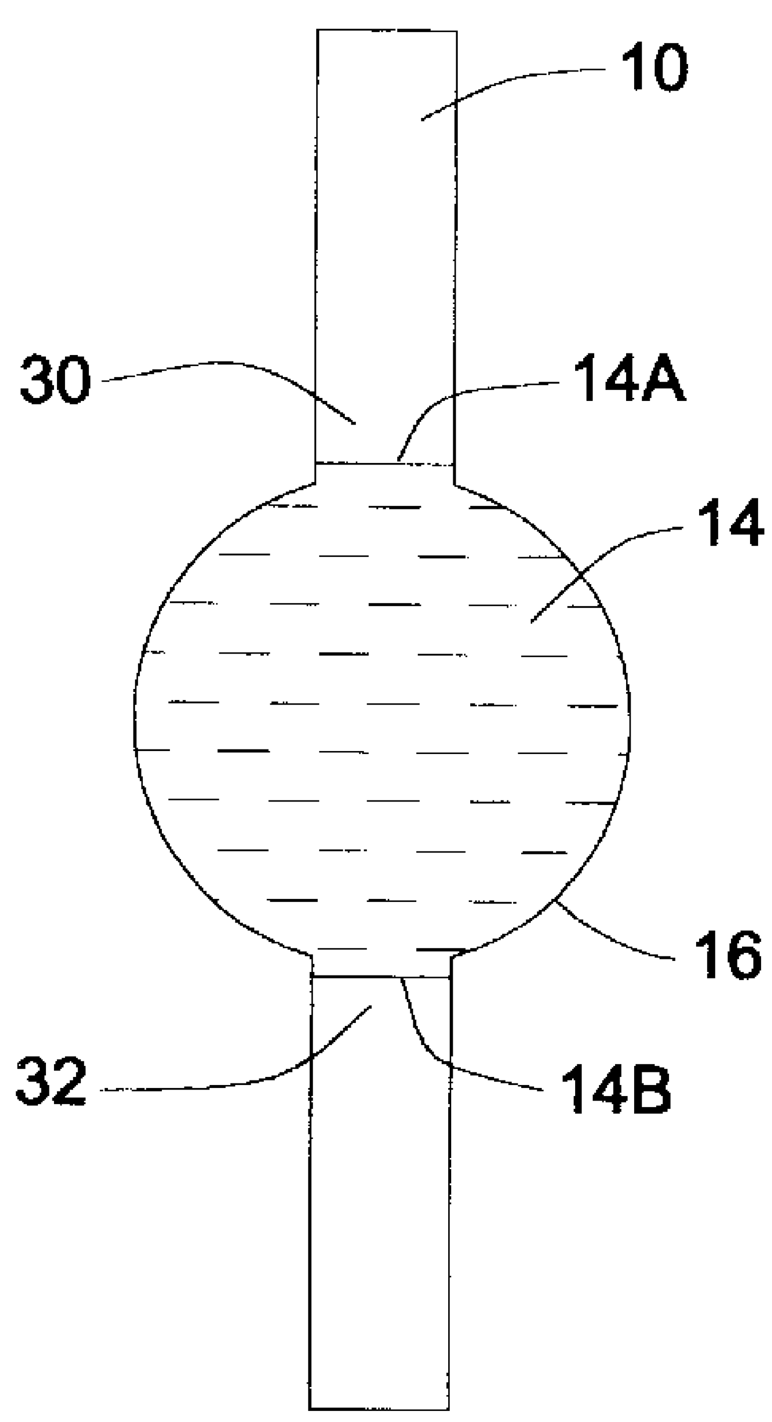


FIG. 4A

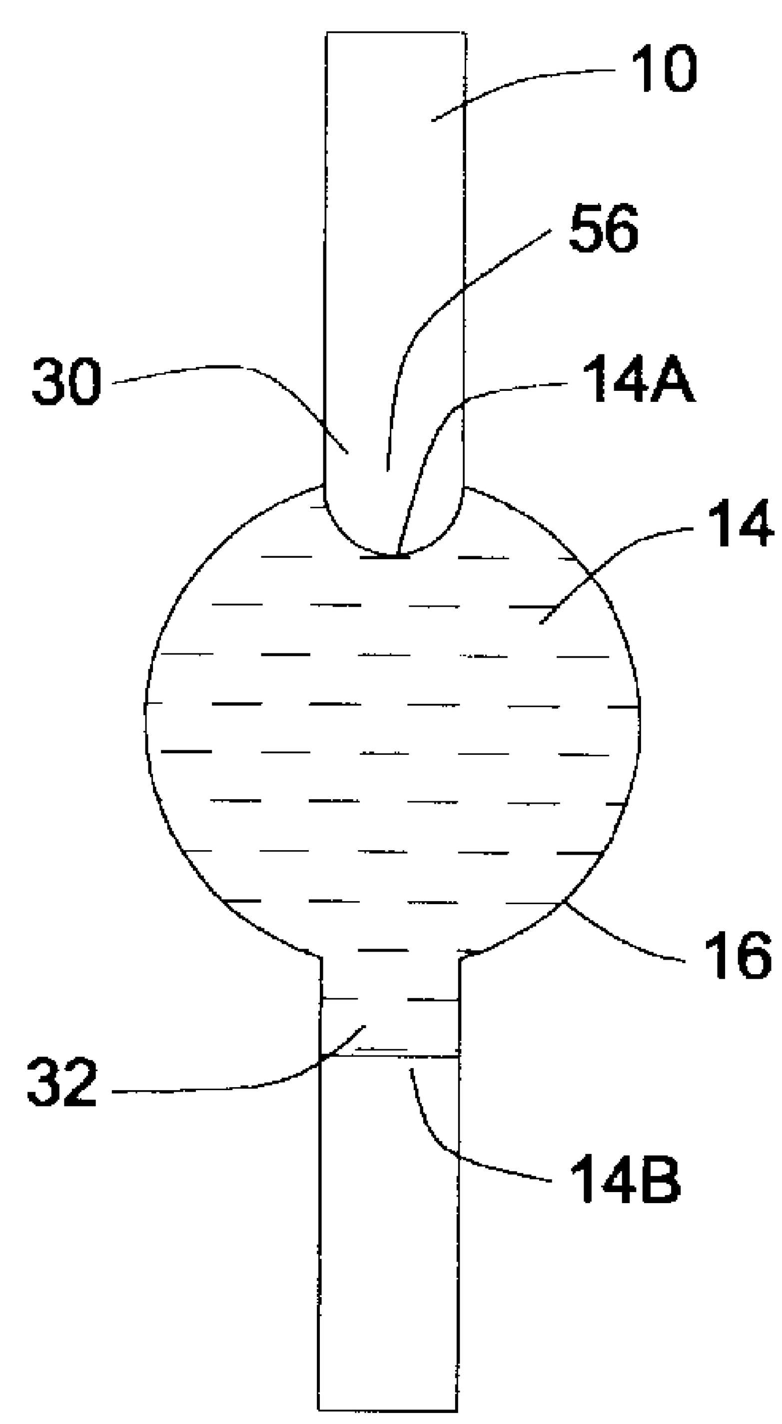


FIG. 4B

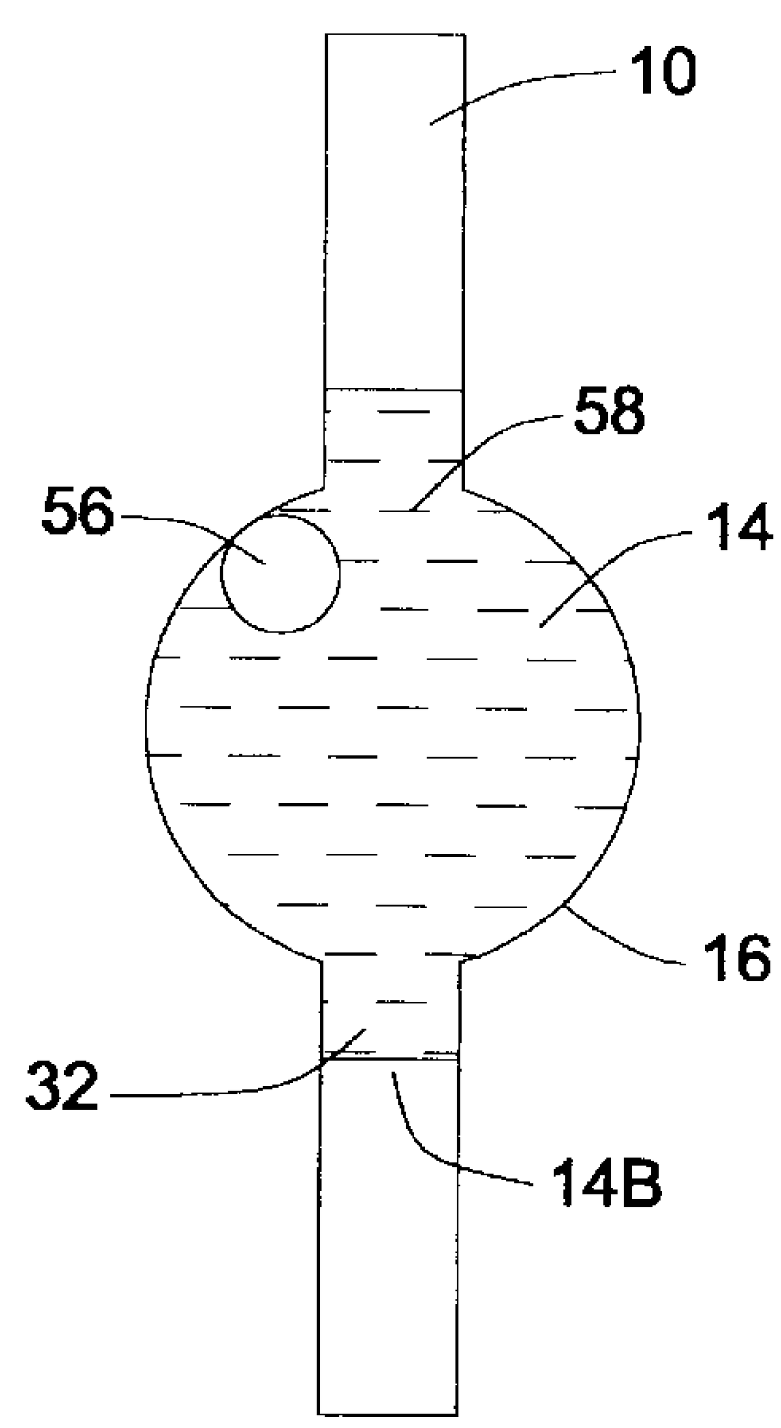


FIG. 4C

FIG. 5A

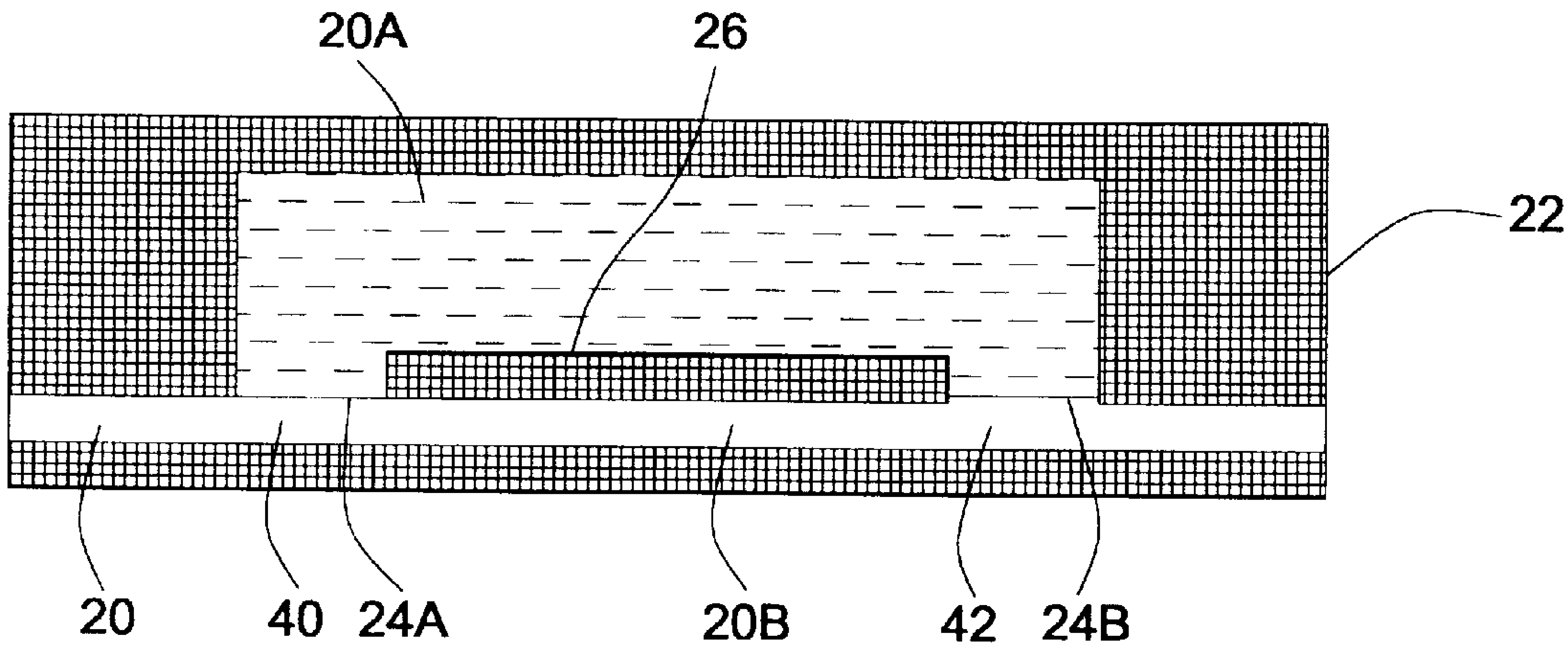


FIG. 5B

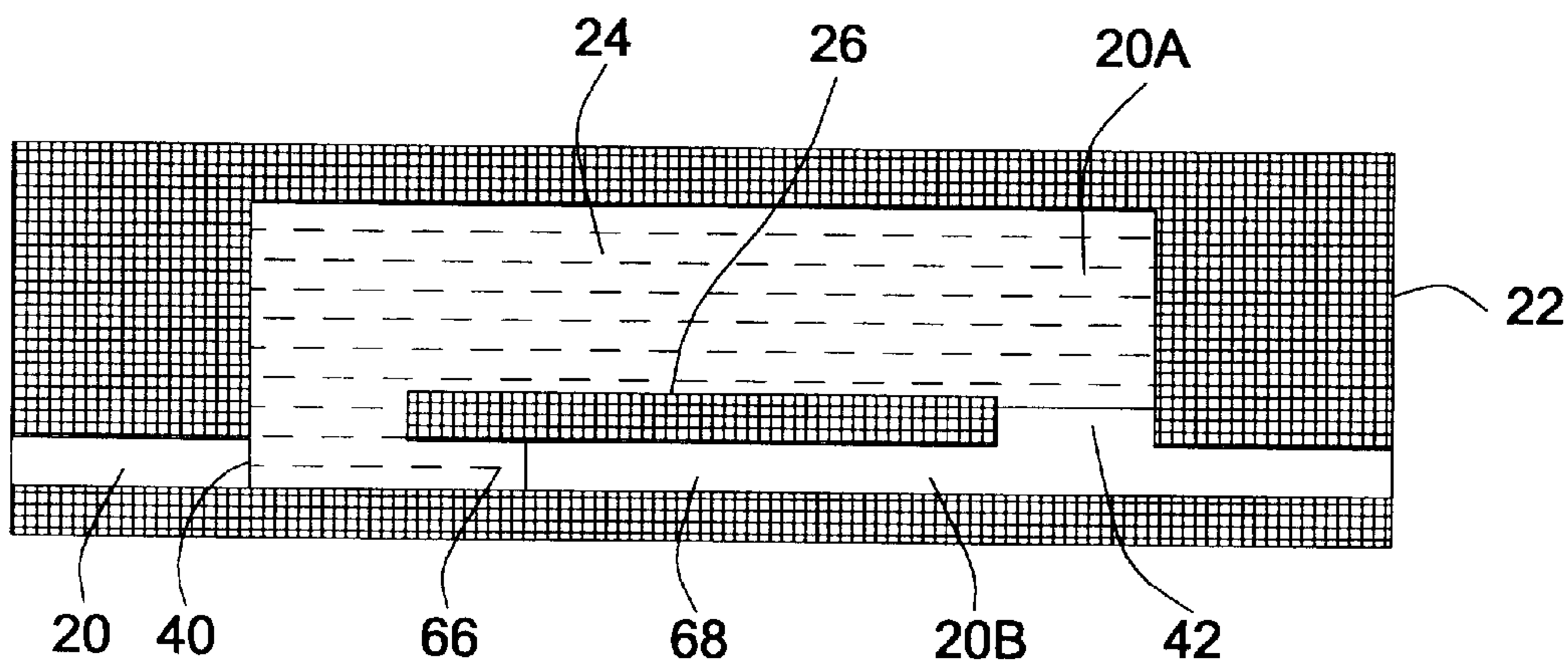
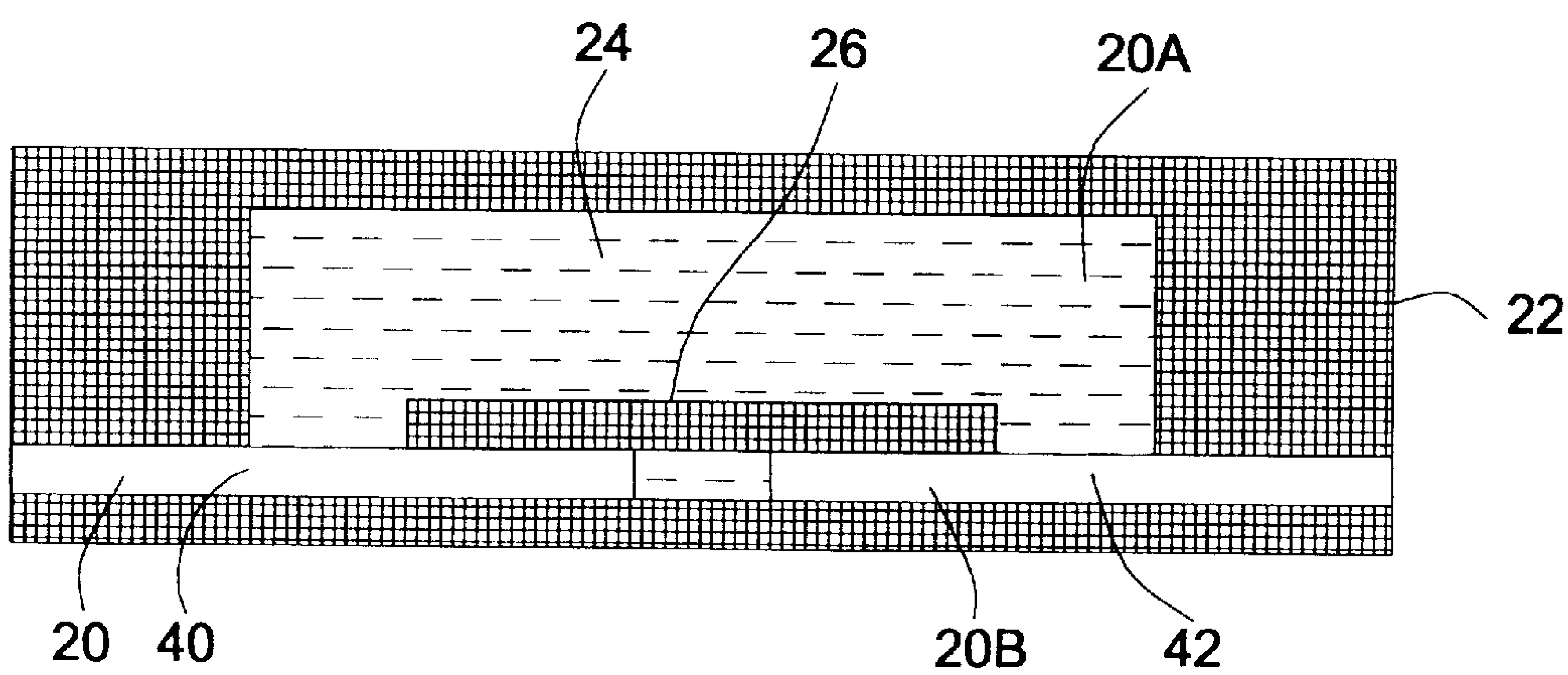


FIG. 5C



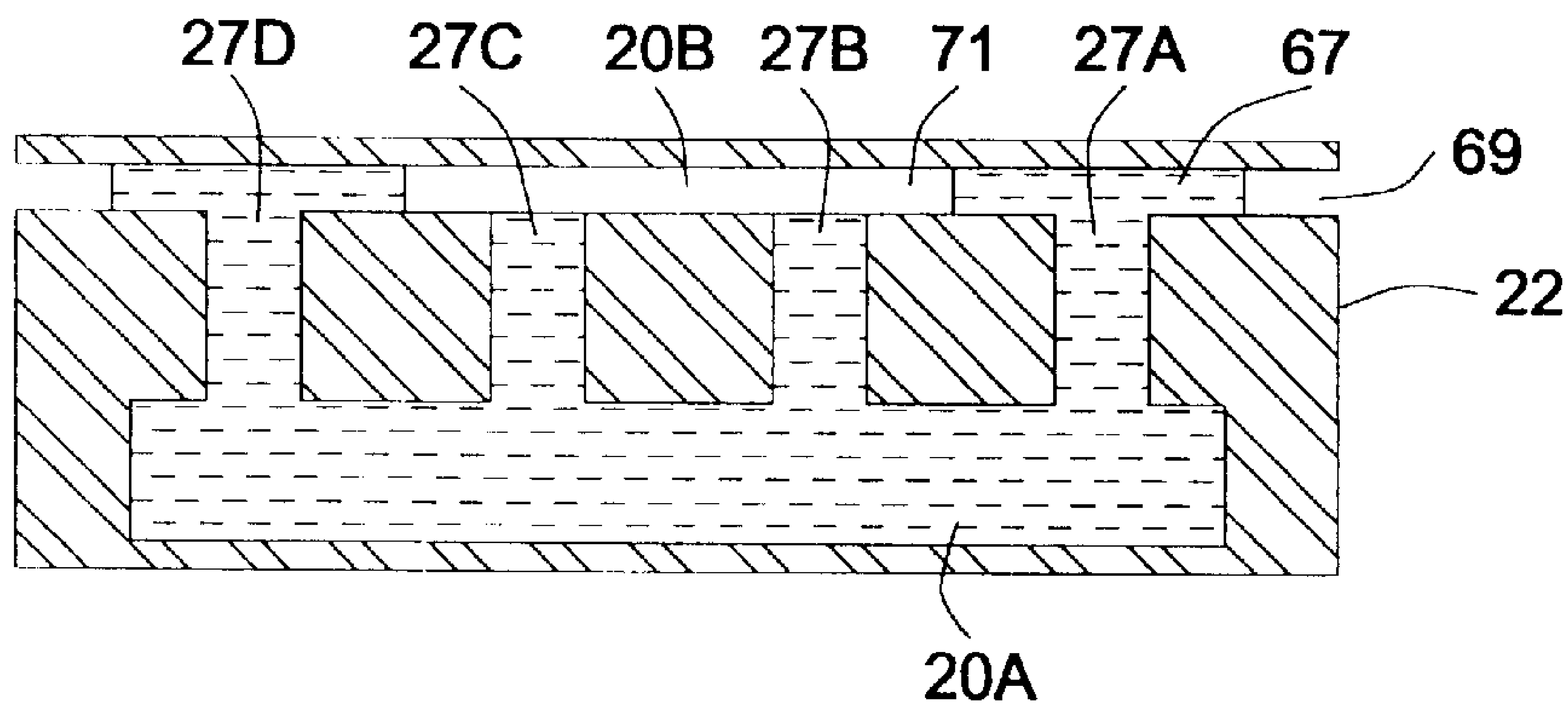


FIG. 6D

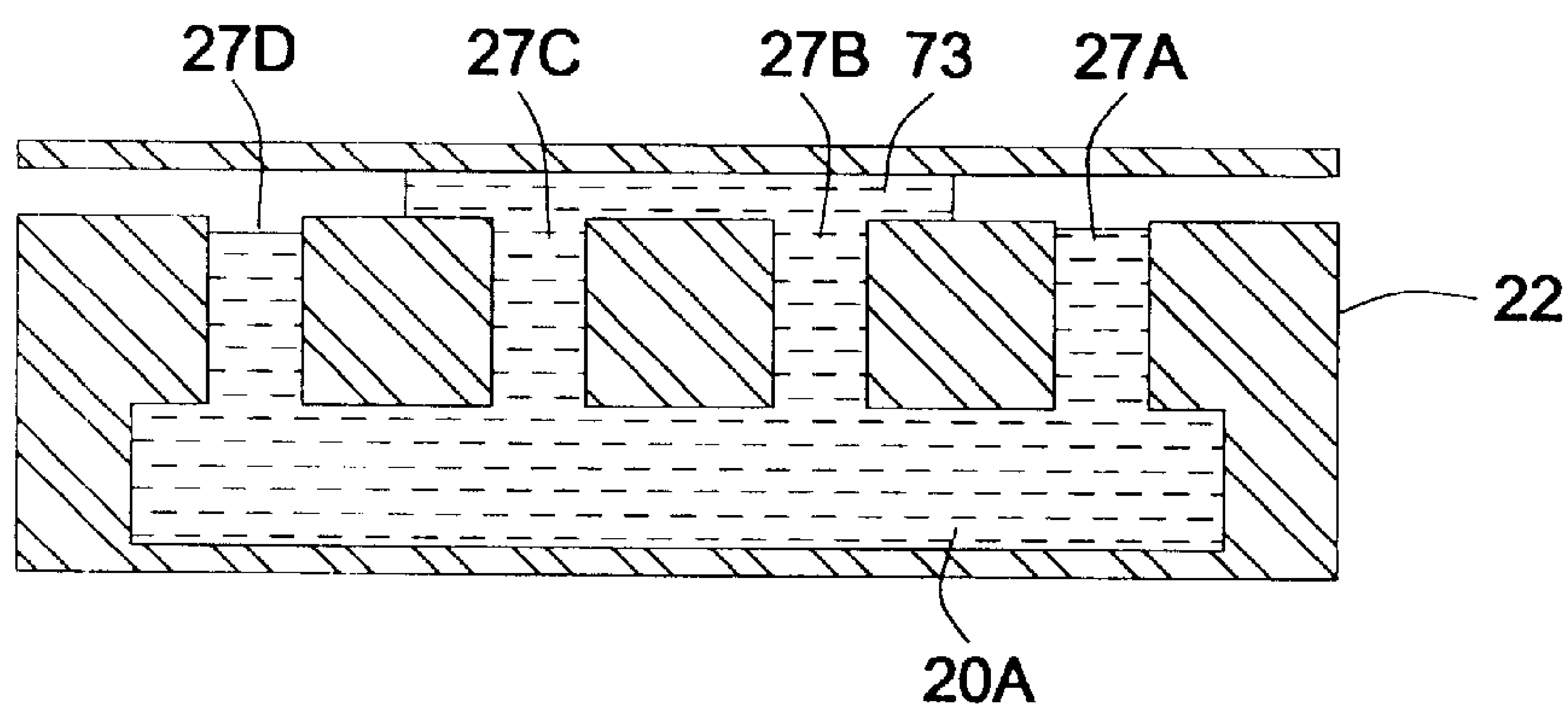


FIG. 6C

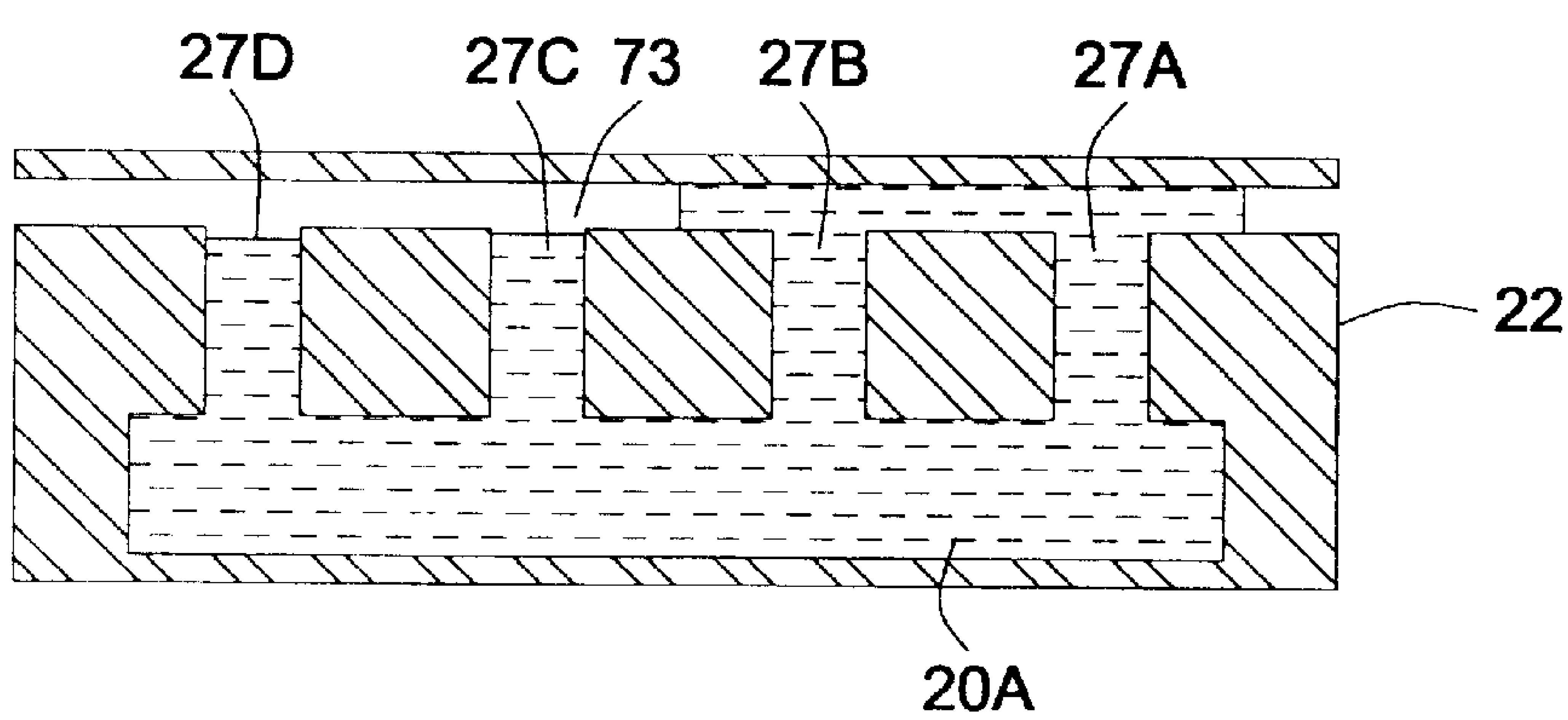


FIG. 6B

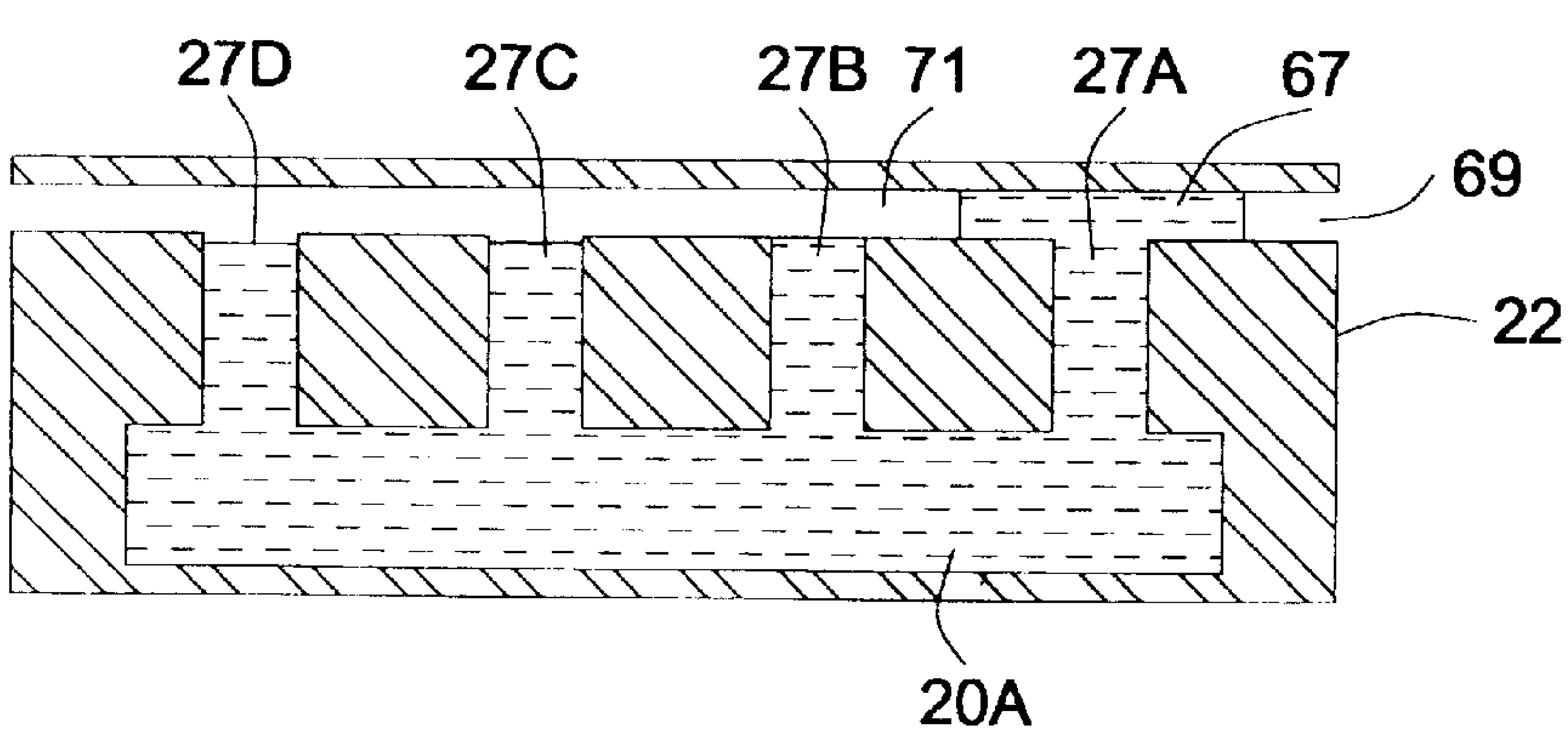


FIG. 6A

FIG. 7B

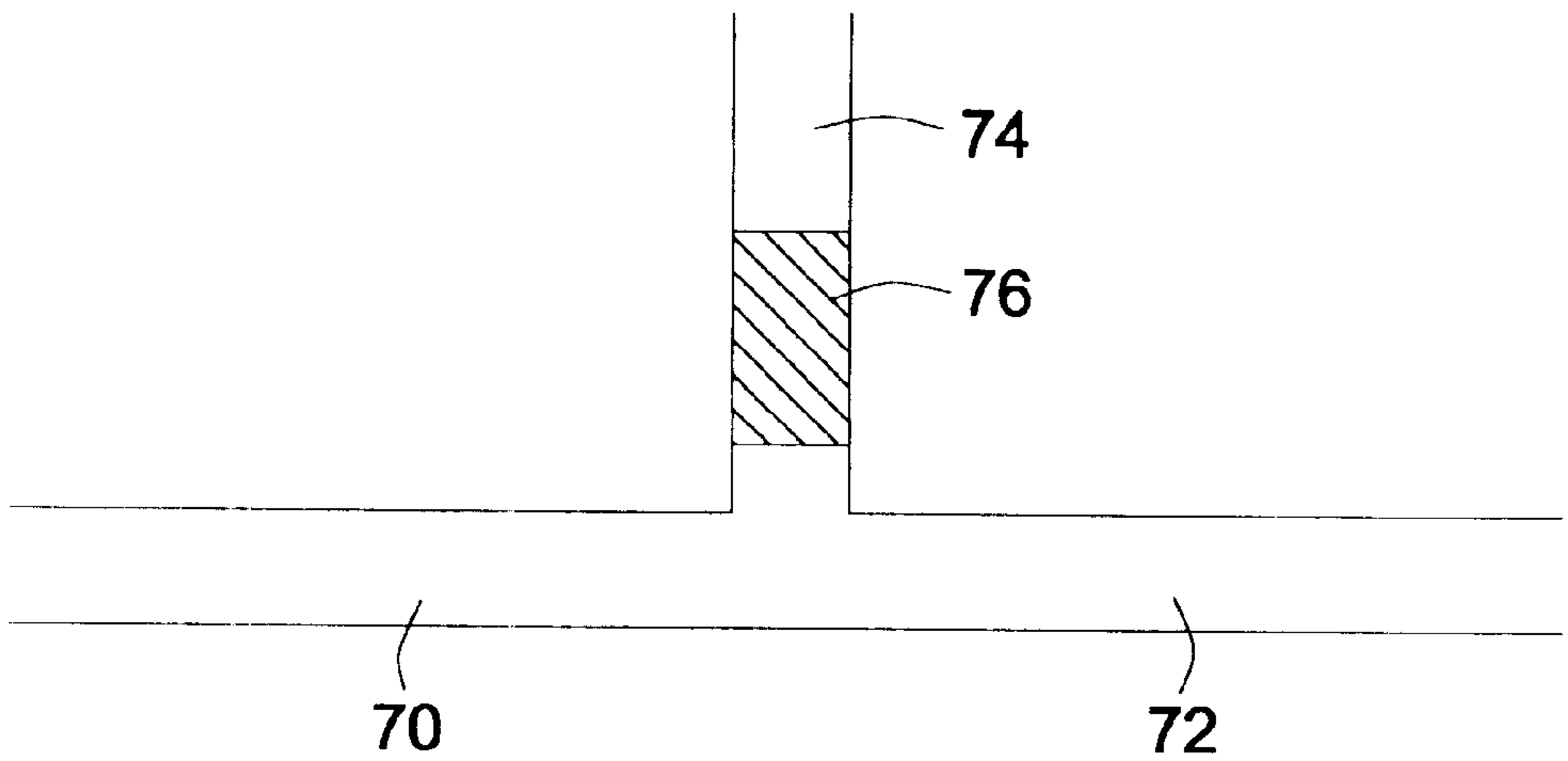


FIG. 7A

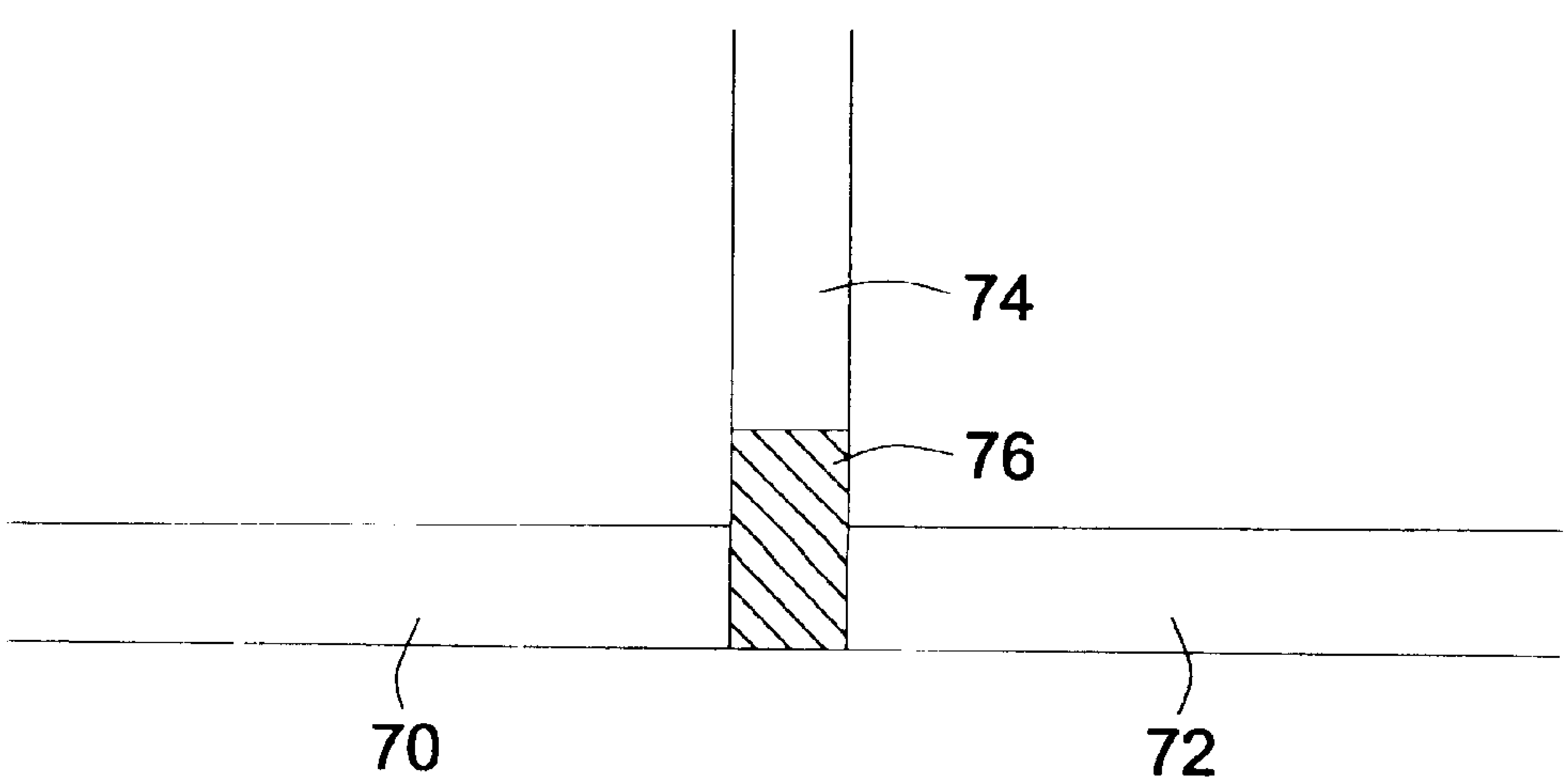


FIG. 8

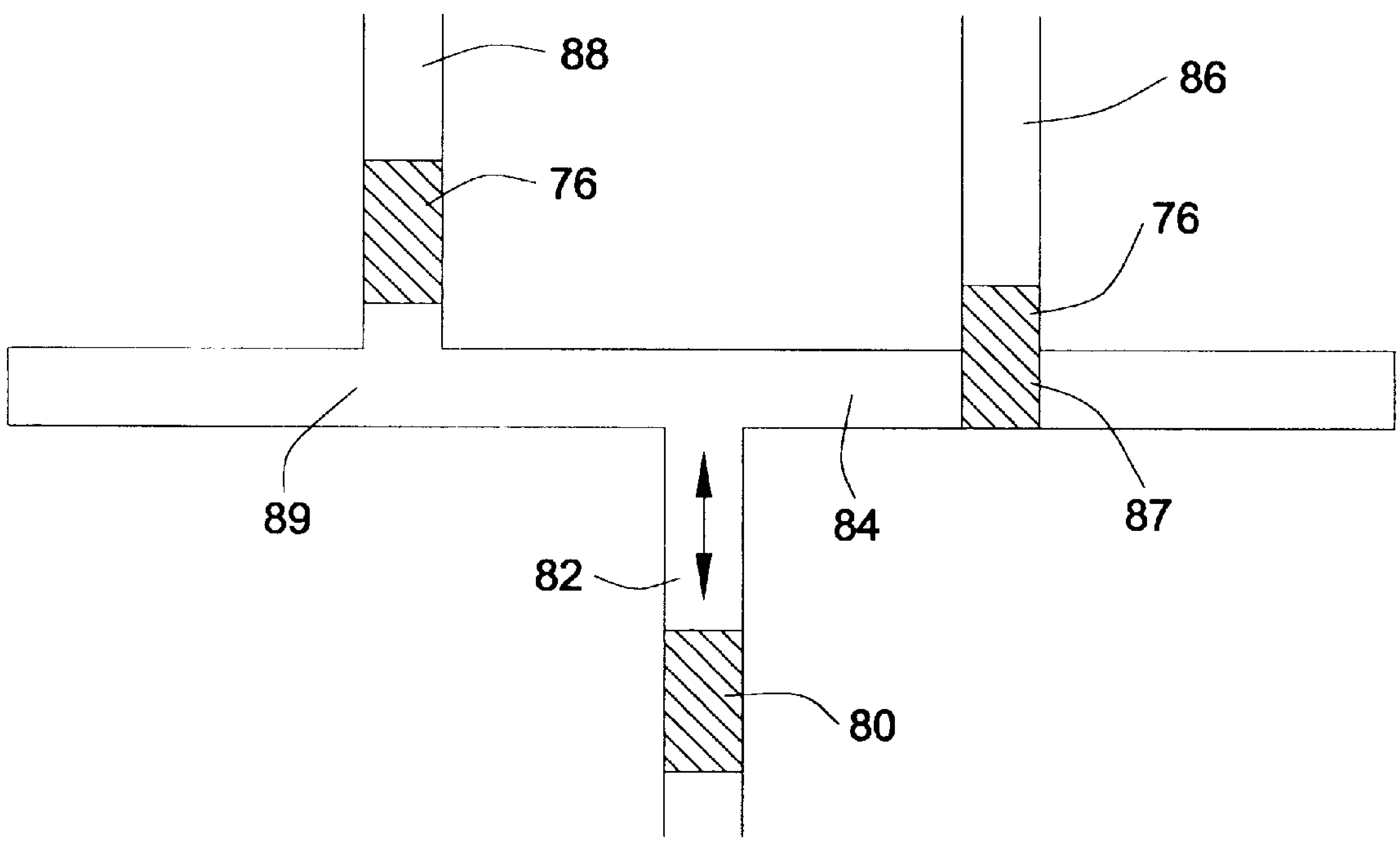


FIG. 8A

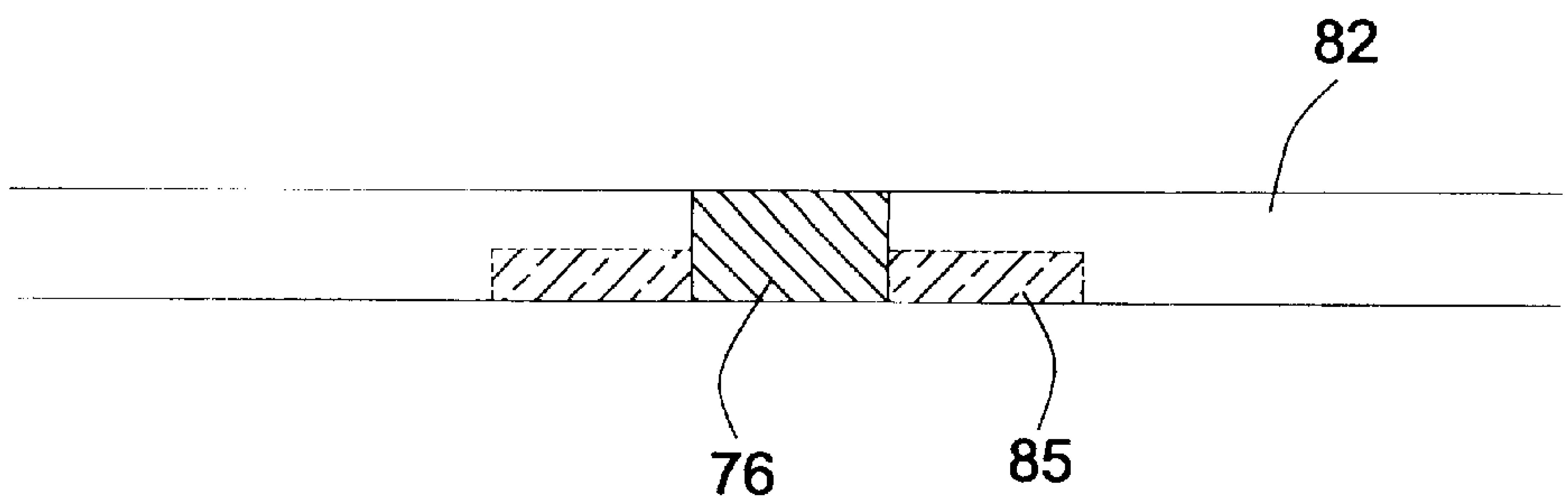


FIG. 10A

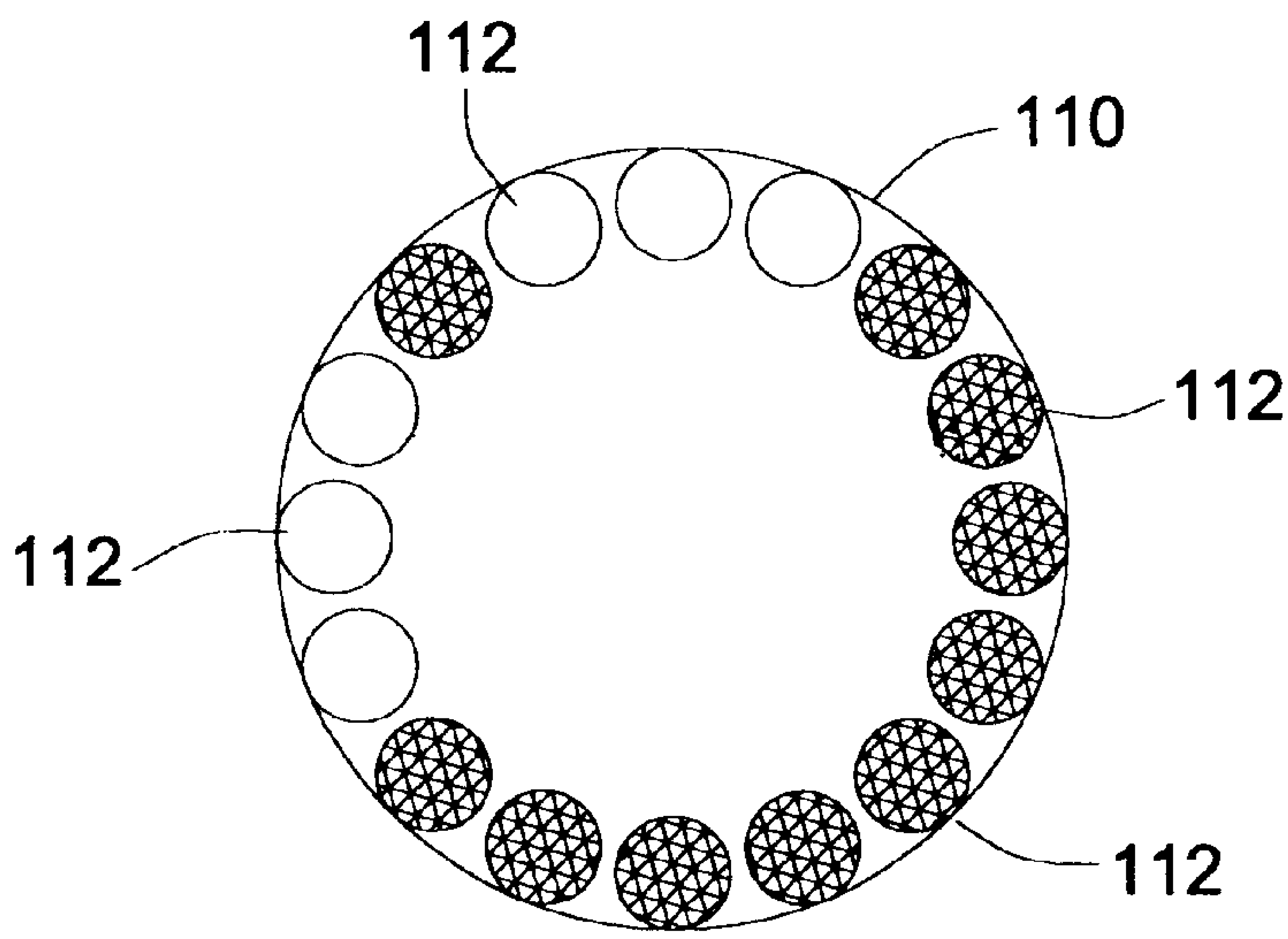


FIG. 9A

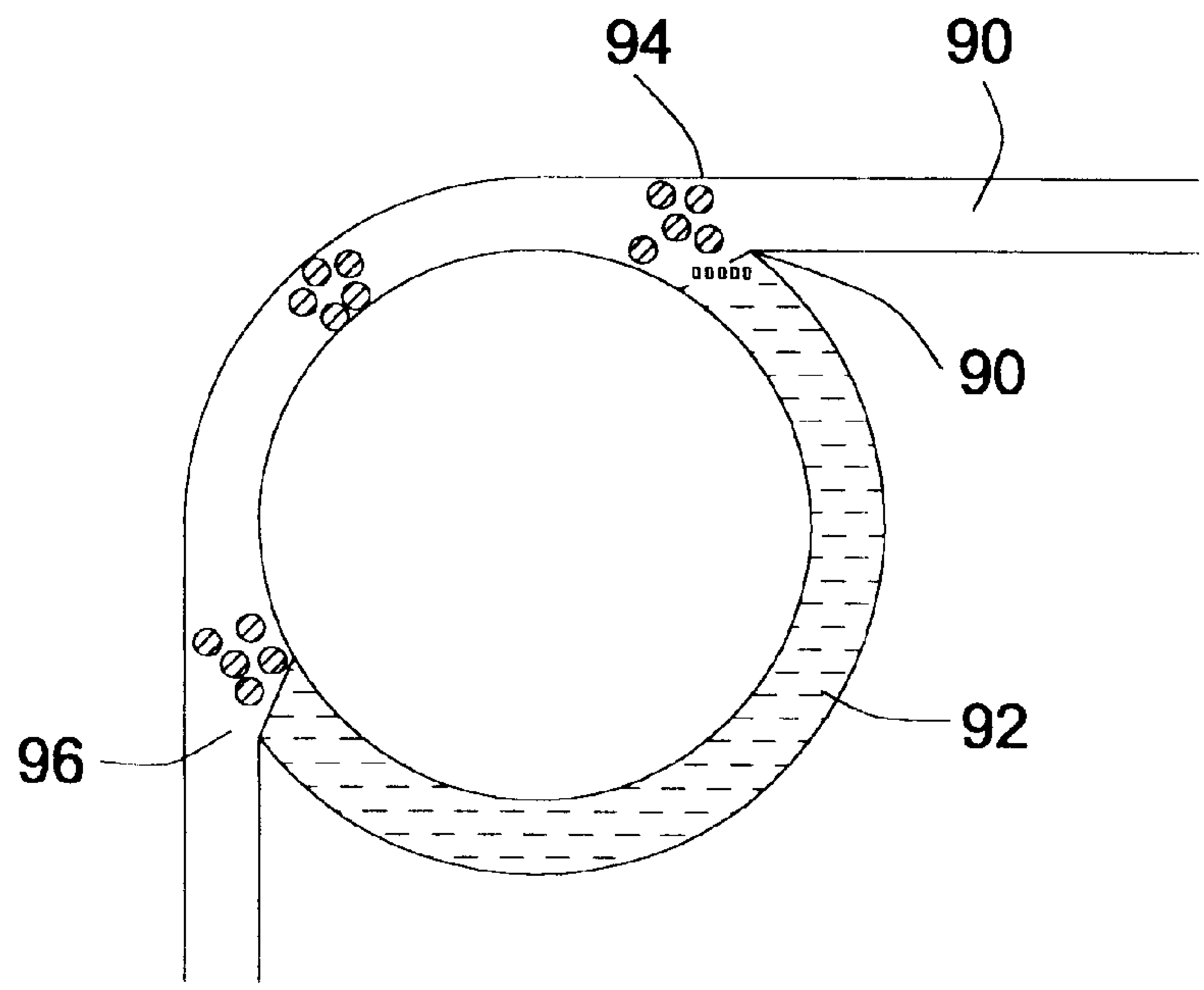


FIG. 10B

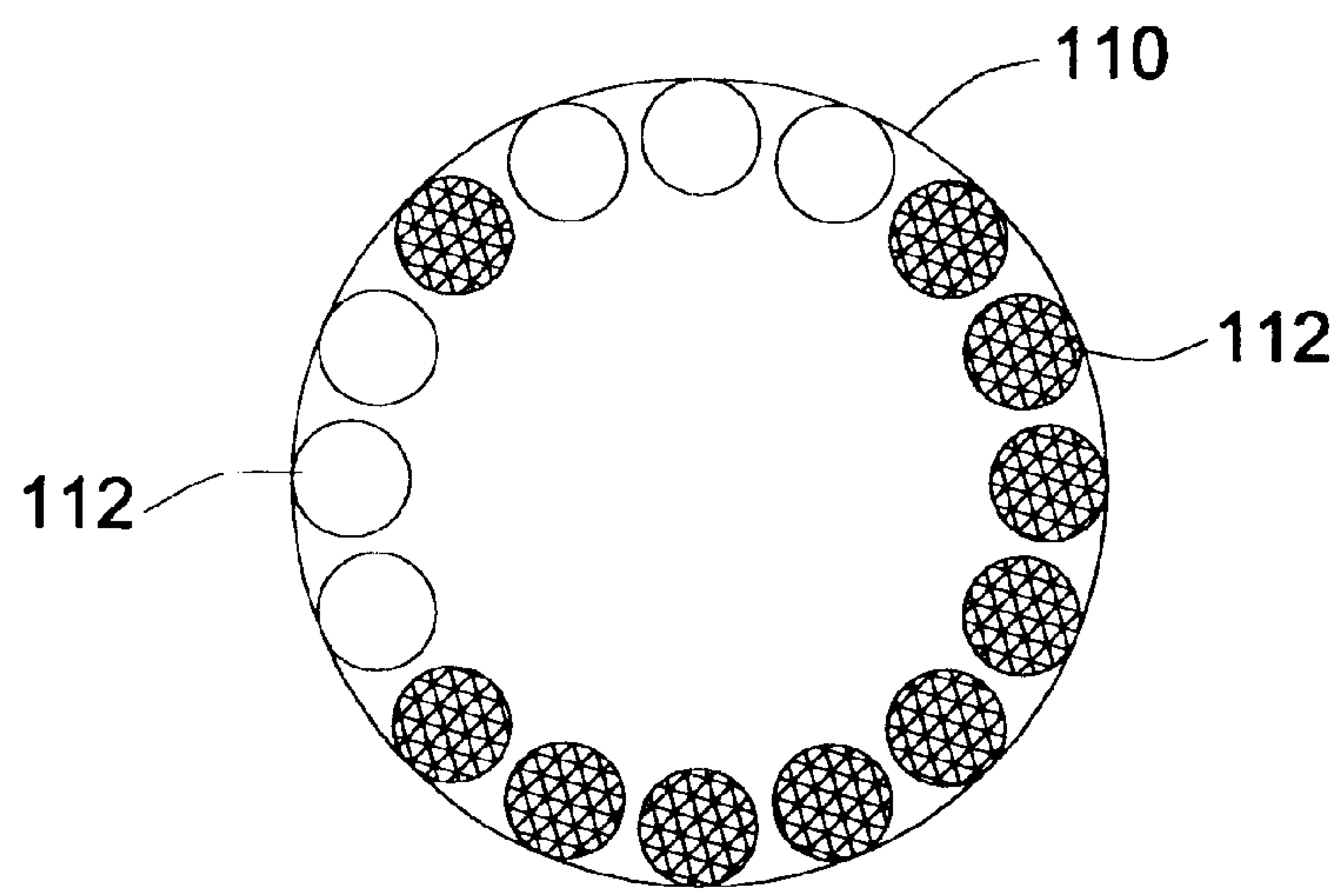


FIG. 9B

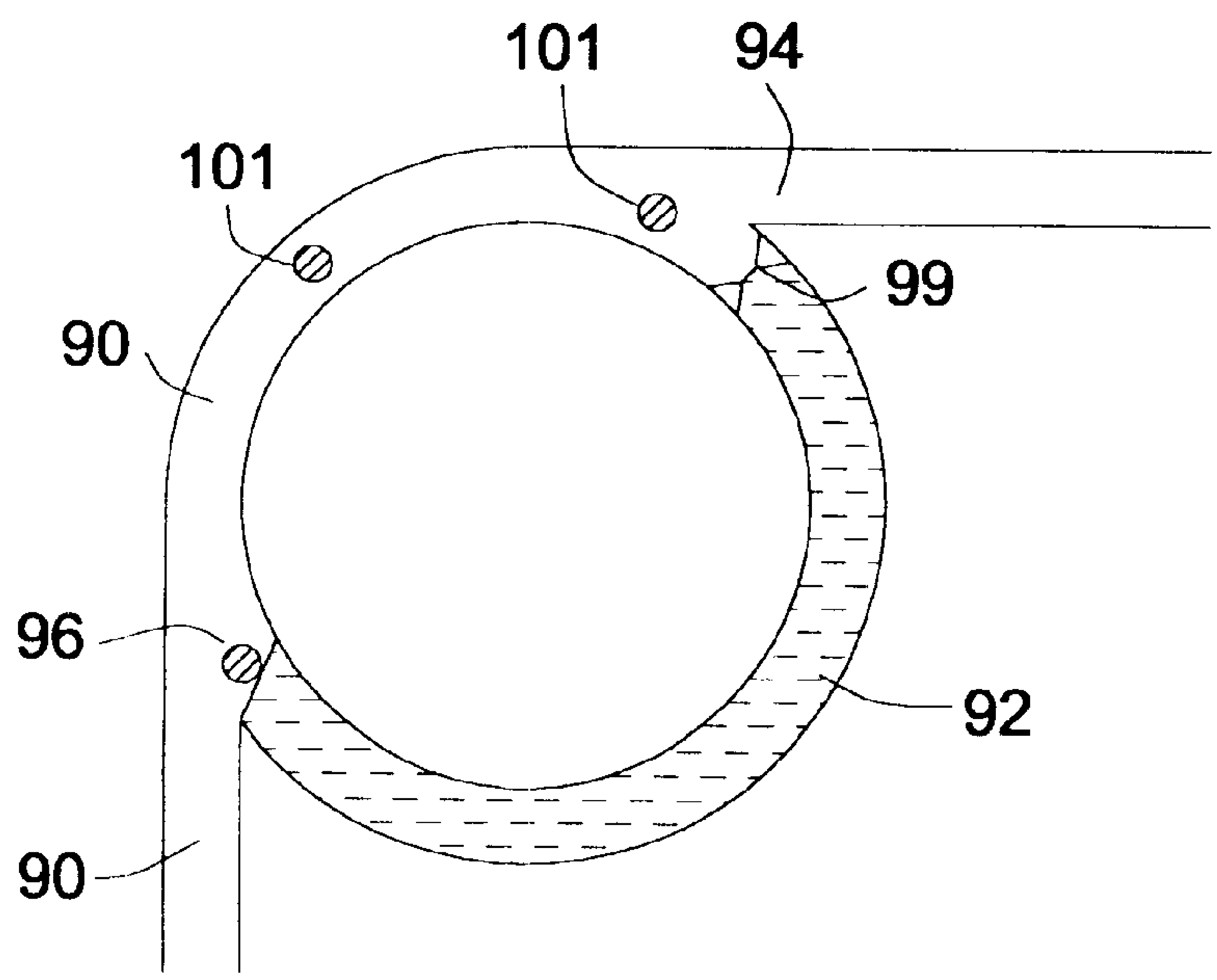


FIG. 10C

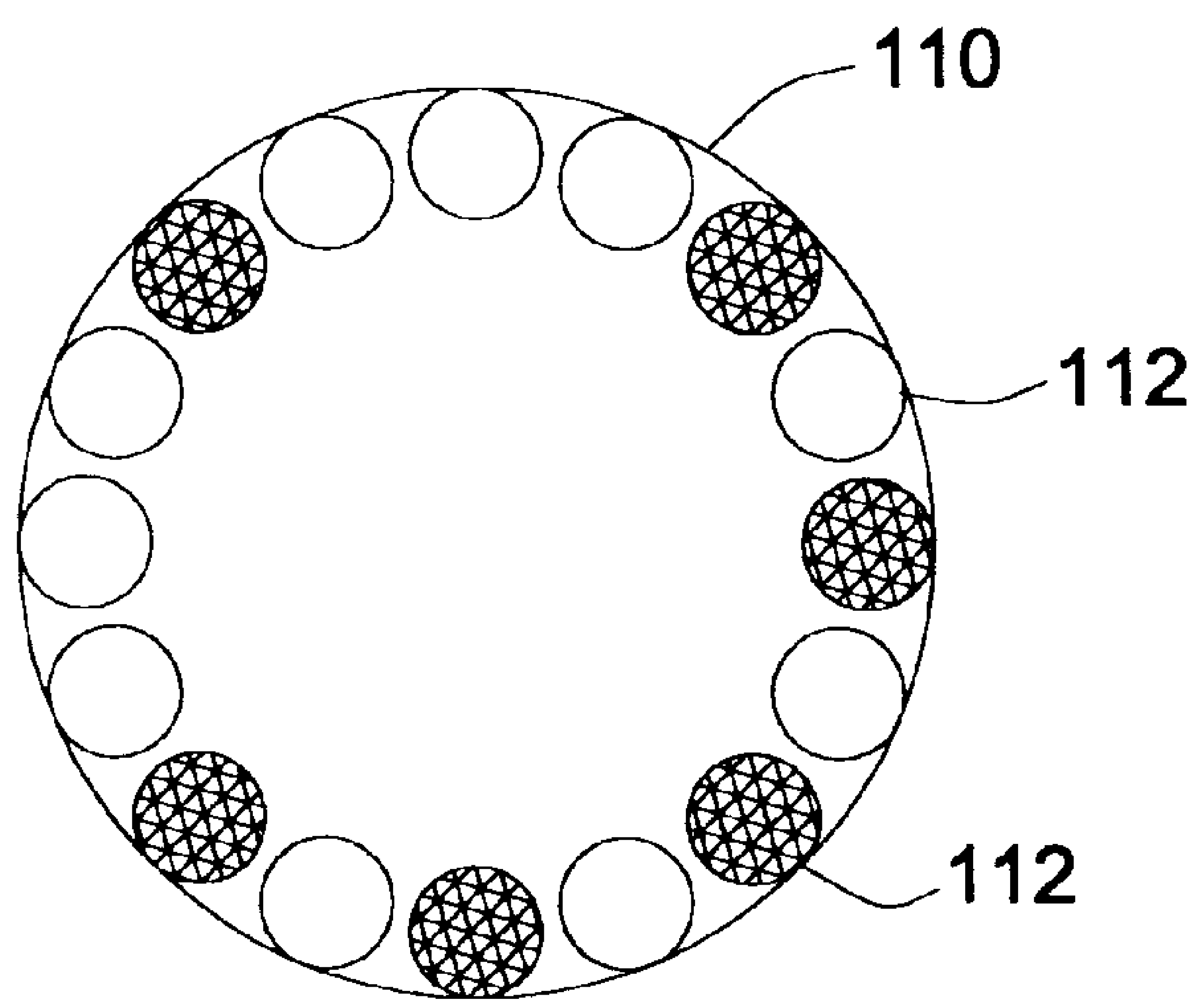


FIG. 9C

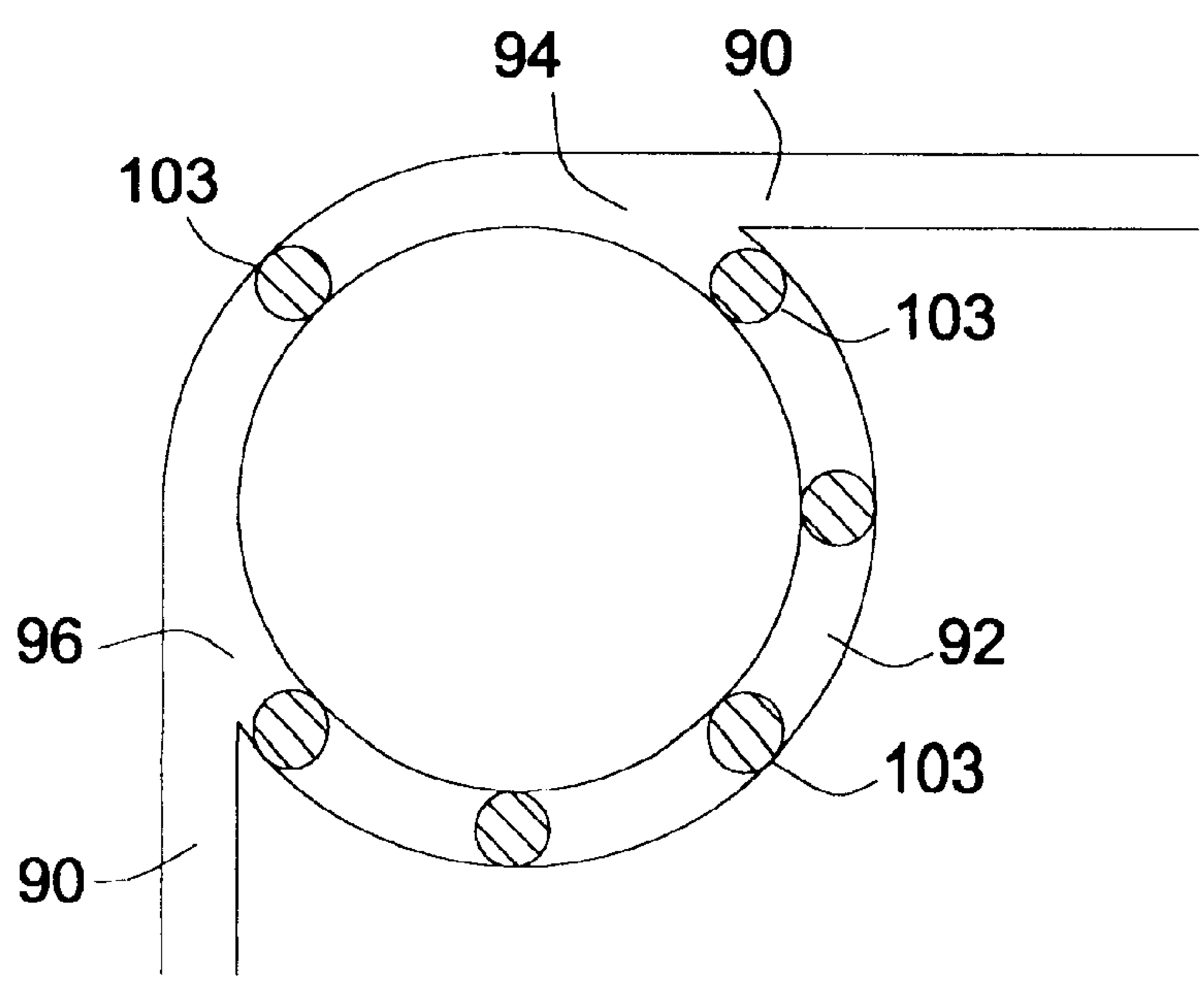


FIG. 10D

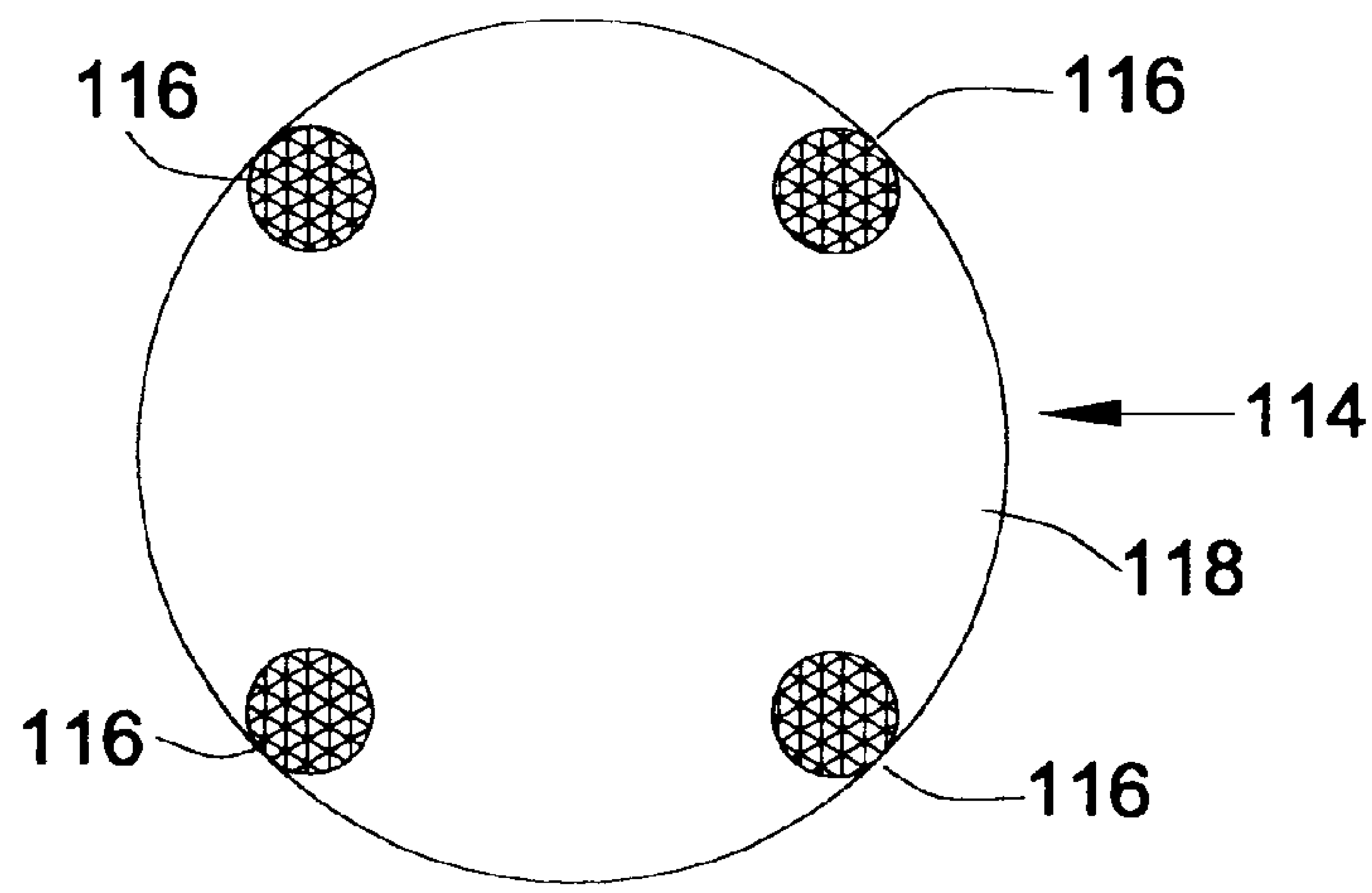


FIG. 9D

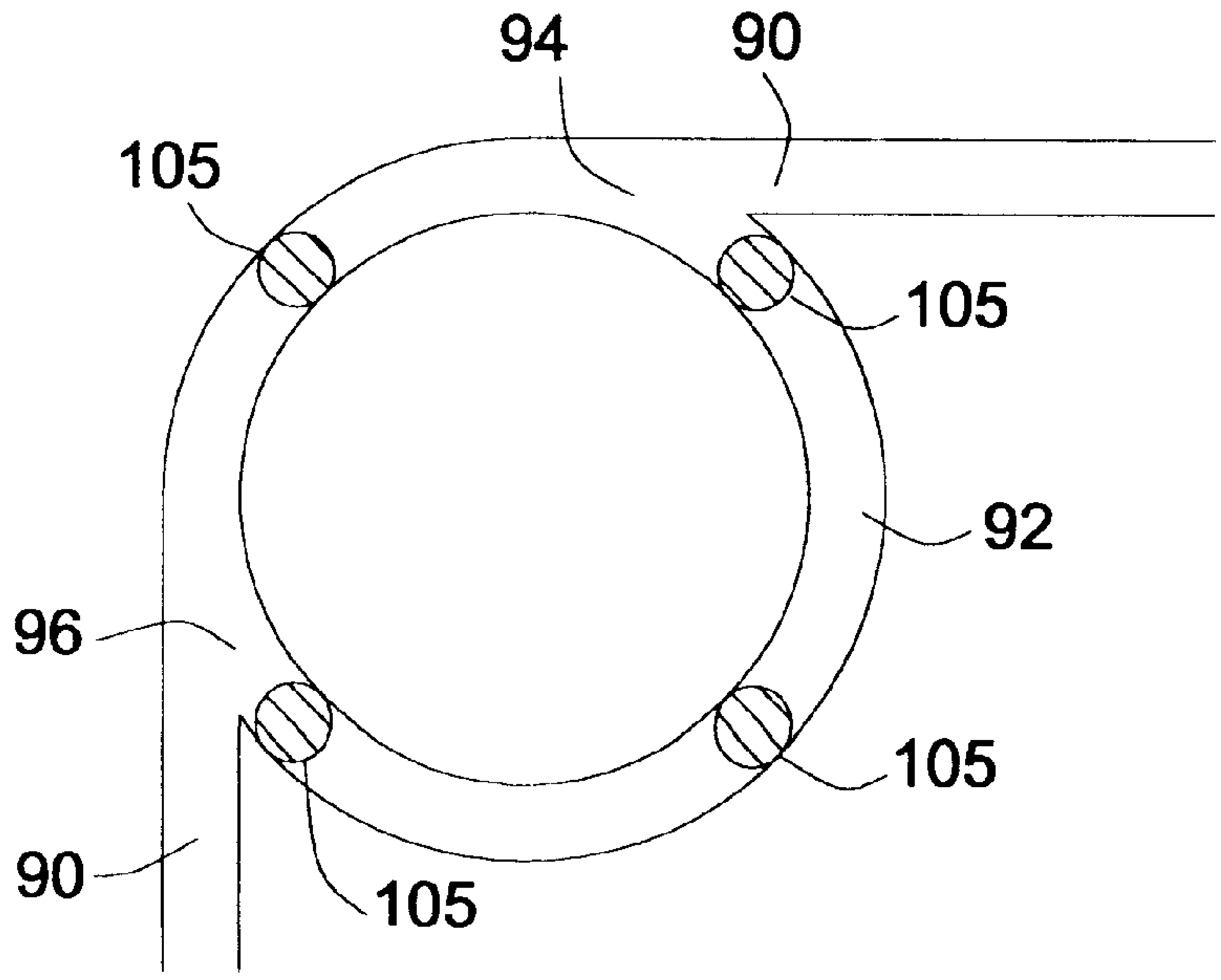
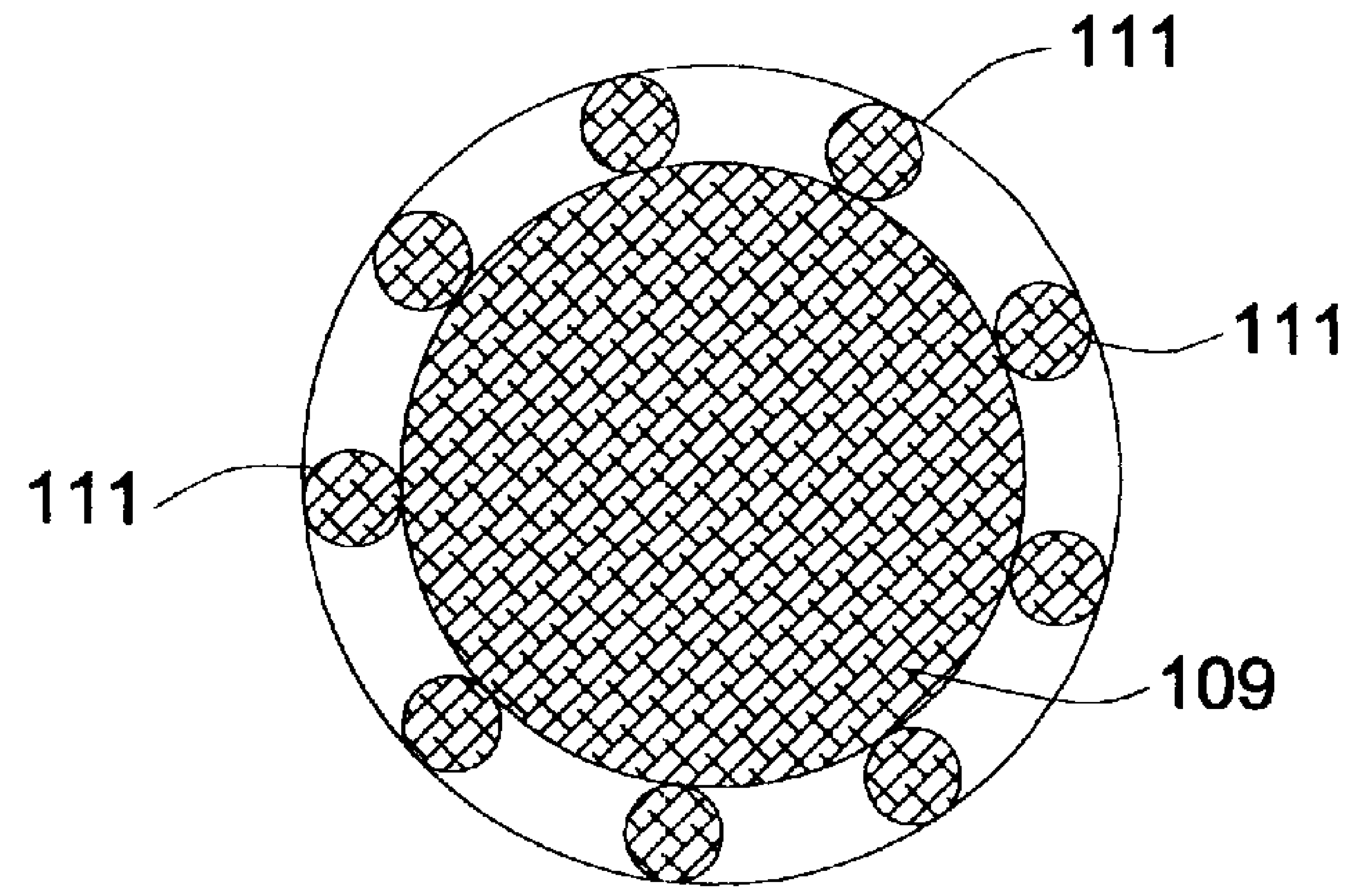


FIG. 10E



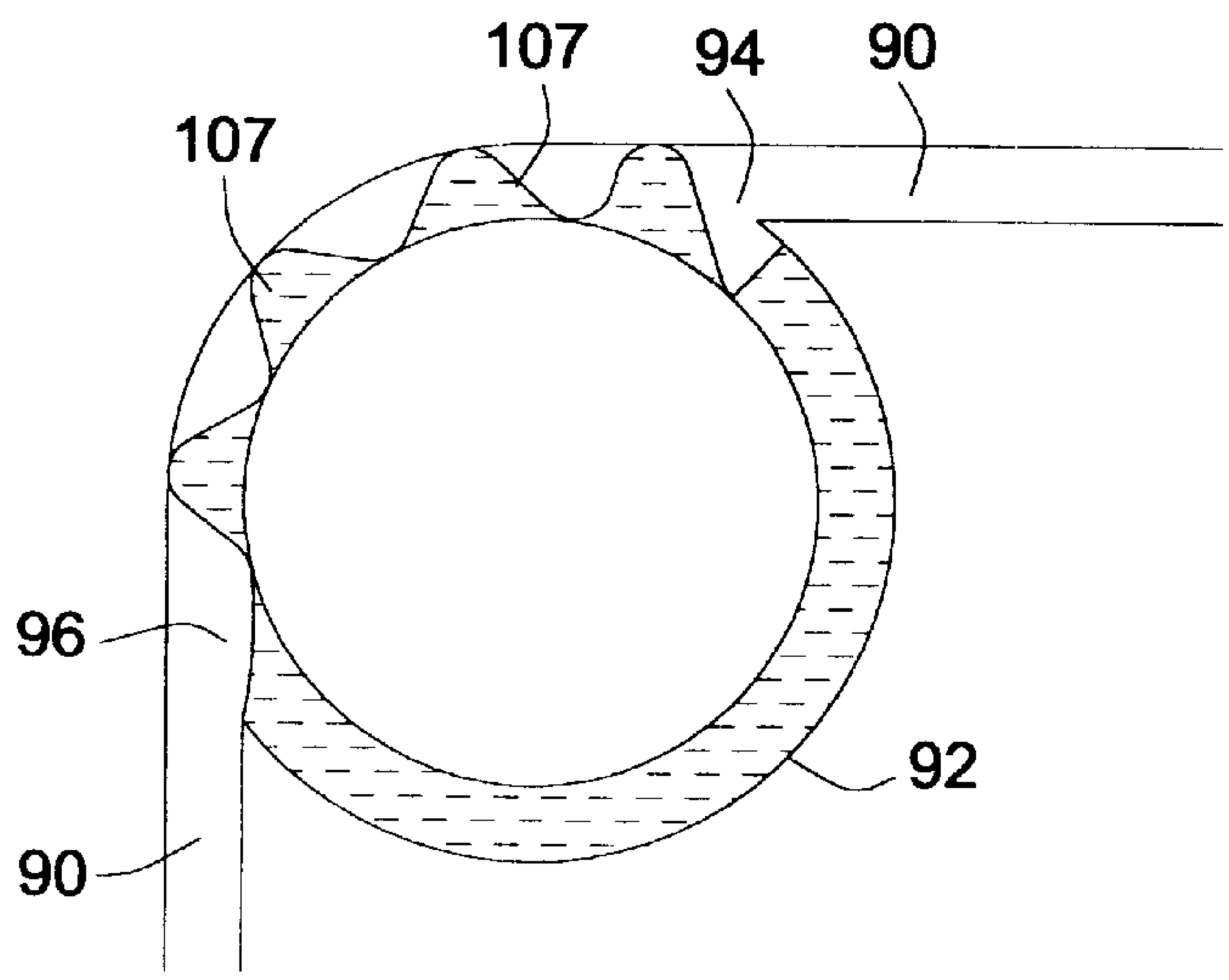
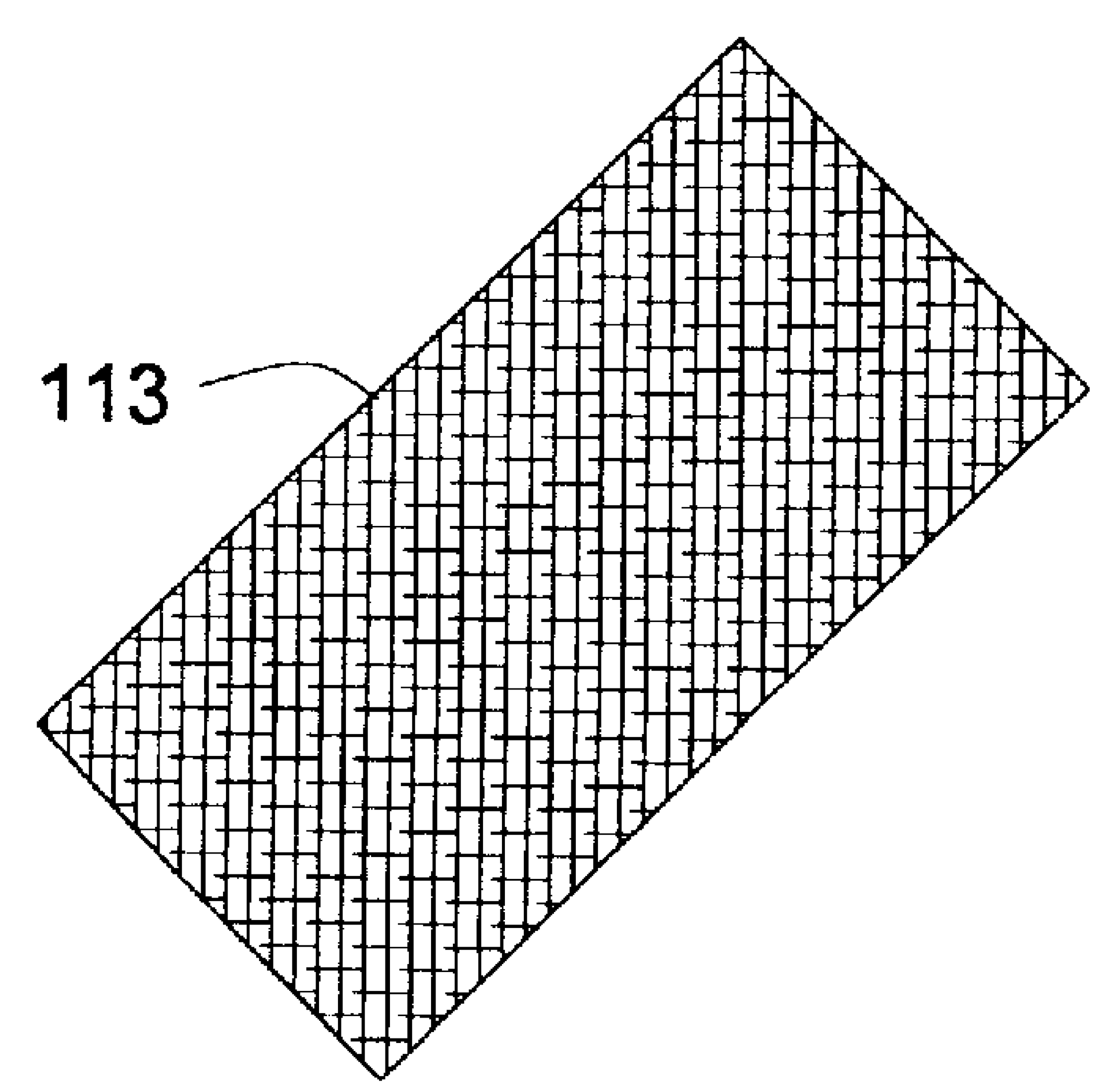


FIG. 9E

FIG. 10F



FLUIDIC DEVICES

FIELD OF THE INVENTION

This invention relates to fluidic devices, and particularly microfluidic devices.

BACKGROUND OF THE INVENTION

Microfluidic devices are becoming increasingly critical to biochemical analysis. These devices may have channels whose cross-sections are in the order of 1 μm to 1000 μm A fluid containing a sample to be analyzed and a reagent for activating the sample are delivered along channels to a reaction zone in the microchip. Pumping of the fluid is often carried out with external pumps, or electrical pumps that rely upon principles such as electroosmosis, electrophoresis and dielectrophoresis. When external pumps are used, problems can arise in both sample and reagent delivery.

For example, in sample delivery, transfer of sample to the chip may result in pressure differentials in excess of the pumping capacity, with resulting pressure fluctuations. In reagent delivery, the channels in the chip must be manually primed with reagent, with risk of cross-contamination.

SUMMARY OF THE INVENTION

There is thus a need for an on chip pump for use with microchips.

The invention provides a device that provides isolation and sample delivery in a microchip while not introducing large dead volumes. In addition, the use of the micropump in the channel allows pre-priming of the microchip, thus reducing the time in which the microchip is exposed to contaminants.

According to a first aspect of the invention, a pump pumps fluid along a channel by moving a drive fluid in the channel under the influence of a force field that is generated externally to the channel. The drive fluid is preferably a ferrofluid, and the force field is preferably a variable magnetic field. Drive fluid, driven by variation of the magnetic field, drives driven fluid through the channel. The drive fluid is recirculated, in one case by rotating the drive fluid within an enlargement in the channel, and in another case by returning the drive fluid along a return channel. The channel is preferably a microchannel in a microchip. The channel and pump may be formed between two plates forming a microchip. The channel may be as small as 1 μm to 100 μm in its cross-sectional dimensions. A valve is formed by using a ferrofluid plug as a movable barrier for fluids in a channel. Methods of pumping fluids by using an in channel drive fluid and exterior drive are also disclosed.

These and other aspects of the invention are described in the detailed description of the invention and claimed in the claims that follow.

BRIEF DESCRIPTION OF THE DRAWINGS

There will now be described preferred embodiments of the invention, with reference to the drawings, by way of illustration only and not with the intention of limiting the scope of the invention, in which like numerals denote like elements and in which:

FIG. **1** is an exploded view showing a first embodiment of the invention;

FIG. **1**A is a section through the embodiment of FIG. **1** along the line **1**A—**1**A;

FIG. **2** is an exploded view showing a second embodiment of the invention;

FIG. **2**A is a section through the embodiment of FIG. **2** along the line **2**A—**2**A;

FIG. **3** is an exploded view showing a third embodiment of the invention;

FIG. **3**A is a section through the embodiment of FIG. **3** along the line **3**A—**3**A;

FIGS. **4**A–**4**C show the manner of operation of the first embodiment of the invention;

FIGS. **5**D–**5**C show the manner of operation of the second embodiment of the invention;

FIGS. **6**A–**6**D show the manner of operation of the third embodiment of the invention; and

FIGS. **7**A and **7**B show operation of an exemplary valve for use with the invention;

FIG. **8** shows an embodiment of the invention as applied to pumping with a reciprocal motion in a microchip;

FIG. **8**A shows how a plug may be stretched to provide differential pumping in opposite directions;

FIGS. **9**A–**9**E show schematically embodiments of the invention in which drive fluid is recirculated around a recirculation channel; and

FIGS. **10**A–**10**E show magnetic drives for the embodiments of FIGS. **9**A–**9**E respectively, with FIG. **10**F showing in addition a permanent magnet that forms part of the drive shown in FIG. **10**E.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

Referring to FIG. **1**, a channel **10** extends through a body **12** and may be formed such as by etching or laser ablating the channel in a base plate **11** and covering **10** the base plate **11** with a cover plate or lid **13**. The channel **10** may have cross-sectional dimensions in the order of 1 μm to 1000 μm, preferably in the range 1 μm to 100 μm. Such devices are known as microchips, and conventional micromachining methods may be used to make the channels. The channel **10** may be straight, but it is preferred to form a reservoir in the channel **10** for a drive fluid plug **14** such as by forming a cylindrical enlargement **16** as in FIG. **1**. In another preferred embodiment, a channel **20** in body **22** formed of base **21** and lid **23** may be split into two branch channels **20**A and **20**B separated by a wall **26** as shown in FIG. **2**. In a further embodiment shown in FIG. **3**, the wall **26** may have passages **27**A–**27**D connecting the channel branches **20**A and **20**B in several places.

Referring as well to FIGS. **4**A–**4**C and **5**A–**5**D, a drive fluid plug **14** or **24** occupies the enlargement **16** or channel **20**B respectively. The drive fluid plug **14** has interfaces **14**A, **14**B with driven fluid in respective spaced apart portions **30**, **32** of the channel **10**. The drive fluid plug **24** has interfaces **24**A, **24**B with driven fluid in respective spaced apart portions **40**, **42** of the channel **20**. The portions **30**, **32** of channel **10** and **40**, **42** of channel **20** are spaced sufficiently to form an adequate stroke for the pump, such as 1 cm.

The drive fluid may be any fluid that is capable of being moved by forces applied by a drive exterior to the channel. For example, the drive fluid is preferably a ferrofluid. A ferrofluid is any fluid that is capable of being moved around under the influence of a magnetic field. When the drive fluid is a ferrofluid, the body **12** should be made of a non-magnetic material at least in areas adjacent to the enlargement **16** or branch channels **20**A and **20**B.

Drives **50**, **60** for the drive fluid are mounted exterior to the channels **10**, **20** respectively. The drives **50**, **60** may be attached such as by clamps to the bodies **12**, **22**, or each may be held in a separate frame. The drives **50**, **60** should be close enough to the bodies **12**, **22** that the force field may drive the drive fluid. The drives **50**, **60** are configured to isolate a driven fluid segment from the portions **30**, **40** respectively of the channels **10**, **20** and drive the driven fluid segment to the portions **32**, **42** of the channels **10**, **20**. When the drive fluid is a ferrofluid, the drives **50**, **60** are magnetic field generators such as electromagnets.

In the example shown in FIG. **1**, the drive **50** is a rotatable magnet or electromagnet with an initially weakly magnetized area **52** and an initially more strongly magnetized area **54**, the remainder of the magnet being moderately magnetized. The drive **50** may be mounted on a shaft **18** of a conventional stepper motor **17**. Power and control for the electromagnetic areas **52** and **54** may be supplied by a power control module **19**.

To facilitate the variability of the magnetization of the areas **52** and **54**, it is preferably that they be elecromagnets. When the magnet **50** is located over the cylindrical enlargement **16** in the channel **10** with the weakly magnetized area adjacent the portion **30** of the channel **10**, drive fluid is pulled away from the weakly magnetized area to alter the interface **14**A and form a pocket in the drive fluid as shown in FIG. **4**B. Driven fluid enters the pocket from the channel **10**. The driven fluid segment **56** in the pocket is isolated from the driven fluid in the portion **30** of the channel **10** as shown in FIG. **4**C with a drive fluid barrier **58** between the driven fluid segment **56** and driven fluid in the portion **30** of the channel **10**. When the magnet **50** is rotated, the drive fluid barrier **58** rotates with the magnet **50** and along with the fluid in the grip of the magnet **50** drives the driven fluid segment **56** around the cylindrical enlargement **16** from the portion **30** of the channel **10** to the portion **32** of the channel **10**. The weakly magnetized area is then magnetized to release the driven fluid segment **56** into the portion **32** of the channel **10**. Preferably, when the pocket is formed, the area **54** is energized to draw fluid towards that end of the magnet. When the pocket is released, the strongly magnetized area **54** is preferably deenergized, weakening the field, to allow drive fluid to flow towards the pocket and drive the driven fluid into the channel **10** at area **32**. As the magnet **50** continues to rotate, the area **54**, which is strongly magnetized during the initial part of the rotation (first 180° of rotation), is made weak, thus forming a pocket that is occupied by a driven fluid segment from portion **30** of the channel **10**. Similarly, area **52** is strengthened, thus attracting the drive fluid towards the end **32**. The magnet **50** may then be continuously rotated to form a flow of driven fluid along the channel, with the degree of magnetization of areas **52** and **54** switching after each half rotation.

In the example shown in FIG. **2**, the drive **60** includes a permanent magnetic strip **70** which is placed exterior to the body **22** over the channel **20**A and individual magnets **61**–**64** over the channel **20**B. This magnetic strip **70** holds the driven fluid in the channel **20**A. A series of electromagnets **61**–**64** are placed exterior to the body **22** between the portions **40** and **42** of the channel **20**B. The operation of the pump shown in FIG. **2** may then be understood from the explanation that follows and FIGS. **5**A–**5**C.

In FIG. **5**A, the electromagnet **61** is strengthened, and the other electromagnets weakened to pull drive fluid into the channel **20**B and form a drive fluid barrier **66** in the channel, which isolates a driven fluid segment **68** from drive fluid in the portion **40** of the channel **20**B. The electromagnets **61**–**64** are then strengthened sequentially so that a localized strong magnetic field moves along the channel **20**B from the portion **40** to the portion **42** of the channel **20**B. This localized strong magnetic field drives the drive fluid barrier **66** along the channel **20**B, separating it from the main drive fluid reservoir in the channel **20**A. As the electromagnets **61**–**64** are successively strengthened, the drive fluid barrier **66** reaches the end of the pump stroke and returns to the drive fluid reservoir in channel **20**A at the interface **24**B. As the series of electromagnets **61**–**64** are repeatedly strengthened in succession, a flow of driven fluid is formed along the channel.

In the embodiment of the invention shown in FIGS. **6**A–**6**D, instead of moving the drive fluid plug along the channel **20**B, the drive fluid is brought out from the cross-channels **27**A–**27**B and returned to the drive fluid reservoir through the same channel. Referring to FIGS. **3** and **6**A, magnet **61** is energized to force drive fluid into the channel **20**B at portion **67** through channel **27**A. This forms a barrier between drive fluid in the channel at **69** and **71**, and drives some fluid along the channel towards cross-channel **27**B. Instead of moving the drive fluid along the channel from portion **67**, the magnet **62** is energized to force fluid along channel **27**B into the portion **71**. This displaces driven fluid further along the channel. The process is repeated for channel **27**C. Magnet **63** is energized to force fluid into channel **20**B at location **73**. At the same time, magnet **61** is deenergized, and fluid in portion **67** is returned by attraction of the magnetic strip **70** to the drive fluid reservoir. This process is repeated for magnet **64**, which is energized while magnet **62** is deenergized, as shown in FIGS. **6**C and **6**D. Finally, the process is repeated again by energizing magnet **61**. The effect of moving the drive fluid from channel **20**A into channel **20**B through cross-channels **27**A–**27**D in succession is to drive driven fluid along the channel **20**B.

In the embodiments shown in FIGS. **2** and **3**, filters may be provided in the return path (eg channel **27**D in FIG. **3**) to prevent driven fluid from mixing with the drive fluid, to enhance stability of the colloidal suspension or to remove any contamination of the drive fluid with the driven fluid.

The drive fluid is preferably immiscible in the driven fluid. A range of immiscible ferrofluids are available commercially available, as for example from Ferrofluidics Inc. of Nashua, N.H. USA. If ferrofluids are used, they should not have ferromagnetic particles larger than the channel size. Ferrofluids available from Ferrofluidics Inc. can withstand **1** atmosphere pressure differential, which is adequate for the intended application. Ferrofluids are colloidal suspensions of ultramicroscopic magnetic particles in a carrier liquid, usually used as lubricants or damping fluids. If the ferrofluid is not immiscible in the driven fluid, then some means must be used to maintain the ferromagnetic particles in a stable colloidal suspension.

The drive fluid may also be a dielectric fluid, and the drive is then provided by a strong electric field, preferably oscillating at high frequency.

As shown in FIGS. **7**A and **7**B, a valve may be formed at a junction between three microchannels **70**, **72** and **74** by placing a ferrofluid plug **76** at the junction as shown in FIG. **7**A and moving the ferrofluid plug **76** with a magnetic drive (not shown) into one of the microchannels as shown in FIG. **7**B and allow free fluid flow between the other microchannels.

Referring to FIG. **8**, a drive fluid plug **80** may also be reciprocated to force fluid along a channel **82** in a microchip. Channel **82** intersects with channel **84**, which has branch channels **86** and **88** connected with it at intersections **87** and **89**, the channels **86** and **88** being located on either side of the intersection between channels **82** and **84**. Ferrofluid plugs **76** operate as valves in the manner described in relation to FIGS. **7**A and **7**B. If the intersection **87** is open while plug **80** is moved towards channel **84**, with intersection **89** closed, fluid in channel **84** will be moved in the direction from intersection **89** to **87** and thus pumped along the channel **84**. If the intersection **89** is open while plug **80** is moved away from channel **84**, with intersection **87** closed, fluid in channel **84** will be moved into channel **82** ready for pumping into channel **84** on the next pump stroke of plug **80**.

In a further example shown in FIG. **8**A, a pump may be formed by moving the plug **76** in channel **82** in one direction, with the plug sealing the channel, and then expanding the plug **76** lengthwise along the channel as shown at **85**, thus thinning it and unsealing it from the channel walls, so that on the return stroke, less fluid is driven.

Referring to FIGS. **9**A–**9**E, embodiments of the invention in which drive fluid is recirculated around a loop channel that intersects with the flow channel are shown. The loop channel in each of FIGS. **9**A–**9**E is shown as circular, but it may have any arbitrary shape that allows the drive fluid to be re-circulated.

In FIG. **9**A, main channel **90** carries the driven fluid. A loop channel **92** intersects with the channel **90** along a path between points **94** and **96**. A magnetic drive **110** as shown in FIG. **10**A has electromagnets **112** spaced around the circumference of the magnetic drive. A strongly magnetized electromagnet is indicated by the dark shading in each of FIGS. **10**A–**10**E, and a weakly magnetized electromagnet is indicated by light shading. Each electromagnet may be energized and deenergized. In FIG. **9**A, at the intersection **94** between the loop channel **92** and the main channel **90**, a nozzle is formed by a series of obstructions **98** in the channel **92**. Drive fluid fills the part of loop channel **92** that does not intersect with the channel **90**. All the electromagnets **112** over the loop channel **92** are strongly magnetized. The electromagnets **112** that are situated over the channel **90** are initially weakly magnetized and when it is desired to pump are sequentially activated, with the first electromagnet **112** to be energized being the one over the region **94**. This draws drive fluid from the drive fluid reservoir into the flow channel **90**. As the electromagnets of the magnetic drive that are located over the flow channel **90** are sequentially activated, drops of drive fluid are forced between the obstructions **98** and moved along the main channel **90** from point **94** to **96**, dragging driven fluid by frictional contact. The drive fluid is pulled by the sequential activation of the electromagnets in the magnetic drive into the loop channel **92** while the momentum of the driven fluid forces the driven fluid along the channel **90**, tangentially to the channel **92**. It is preferred to have strong magnetization in the loop channel **92** just beyond the point **96** to ensure recirculation of drive fluid around the loop channel **92**.

In FIG. **9**B, a similar device to the device shown in FIG. **9**A is shown, except the injector obstructions **98** are replaced by a restriction or nozzle **99**, from which large fluid drops **101** are pulled by a localized strong magnetic field, moved along the channel **90** to point **96** and returned to the loop channel **92** for recirculation. The large drops have a size similar to the channel width. Again, the localized strong magnetic field is created by sequential activation of the electromagnets over the flow channel **90**, as illustrated in FIG. **10**B.

In FIG. **9**C the same loop channel **92** and main channel **90** are used. However, fluid in the loop channel **92** is continuously moved around the loop channel as a series of segments **103** by several spaced locally strong magnetic fields. As shown in FIG. **10**C, the magnetic drive is again a series of sequentially activated electromagnets **112**. In this case, the electromagnets **112** are activated sequentially to attract the drive fluid and move it anticlockwise around the loop **92**. Over the loop channel **92**, the electromagnets may alternate in relative magnetic strength. Care must be taken to coordinate activations so that drive fluid does begin moving clockwise. Over the flow channel **90**, the spacing between the activated electromagnets **112** is increased to create suction and pull more driven fluid along the flow channel **90** to be pumped.

In FIG. **9**D, the loop channel **92** and flow channel **90** are the same as in FIG. **9**A. A magnetic drive **114** is formed by several magnets **116** mounted for rotation on a ring or disc **118** driven for example by a stepper motor (not shown in FIG. **9**D). Four permanent magnets **116** may be used. Each electromagnet should be strongly magnetized. As the drive **114** rotates, drive fluid drops **105** are pulled around the loop channel **92** and through the flow channel **90** to drive driven fluid in the flow channel along the flow channel **90**. In FIG. **9**D, it is preferred that channel **90** be slightly wider than channel **92** to accommodate volume changes due to the pressure exerted by the drive fluid.

In FIG. **9**E, loop channel **92** and main channel **90** are the same as shown in FIG. **9**A. In this case, a strong ring shaped magnetic field is formed by a magnetic drive to shape the drive fluid into a ring on the inside of the loop channel **92** with multiple barriers or cogs **107** spaced around the loop channel **92**. The cogs **107** may be continuous around the loop channel **92** or may be generated only in the flow channel **90**. The magnetic drive in this instance is formed by a disc magnet **109** centered in the middle of the circle formed by the loop channel **92** and flow channel **90** with spaced satellite magnets **111** around the periphery of the disc magnet **109**. To create a reservoir of drive fluid in the loop channel **92**, a permanent magnet **113** may be placed over the loop channel **92**. As the magnetic drive rotates (driven for example by a stepper motor), the cogs **107** drive driven fluid along the channel **90**.

The magnets or electromagnets require an active field area commensurate with the size of the channel, but may be larger. For example, magnetic drivers for use with a microchip may be provided by coils with ferromagnetic cores having a diameter of in the order 100 μm. When the magnets are rotated, commercially available stepper motors may be used. The size of the apparatus outside the channels is not a factor in the operation of the pumps. A varying magnetic field may also be created in the channel by varying the distance of a permanent magnet from the channel.

In the embodiment of FIG. **1**, several pockets could be formed in the driven fluid plug by several weak field areas in the magnet, but the more driven fluid that has to be moved in a single rotation, the more drive fluid has to be displaced. An additional reservoir to take drive fluid overflow may be required in this instance.

The pumps shown in FIGS. **1**, **2** or **3** may be connected to a chamber having a small closeable opening at one end. The chamber may be evacuated with the pump to form a vacuum chamber, and samples may be drawn in through the opening for analysis within the chamber, such as by using a mass spectrometer.

A person skilled in the art could make immaterial modifications to the invention described in this patent document without departing from the essence of the invention that is intended to be covered by the scope of the claims that follow.

What is claimed is:

1. A micropump, comprising:

a microchip having a channel extending through the microchip, the channel having cross-sectional dimensions between 1 μm and 100 μm;

a drive fluid plug in the channel;

a driven fluid in the channel having an interface with the drive fluid plug in the channel; and

a drive for the drive fluid mounted exterior to the microchip, the drive being configured to form a changing field that in operation may drive driven fluid along the channel by changing the location of the interface between the drive fluid plug and the driven fluid.

2. The micropump of claim **1** in which the drive fluid forming the drive fluid plug is a ferrofluid formed of a suspension of magnetic particles in a carrier liquid, and the drive is a magnetic drive.

3. The micropump of claim **1** in which the drive is configured to rotate drive fluid entirely around a loop formed in the channel.

4. The micropump of claim **2** in which the drive is configured to form cogs of drive fluid disposed around the loop in the channel.

5. The micropump of claim **1** in which the channel is formed in a base plate and covered by a cover plate.

6. A micropump, comprising:

a microchip formed of a base plate and a cover plate, a channel formed in the base plate that extends through the microchip with the cover covering the channel, the channel having cross-sectional dimensions between 1 μm and 100 μm;

a drive fluid plug in the channel, the drive fluid forming the drive fluid plug being a ferrofluid formed of a suspension of magnetic particles in a carrier liquid;

a driven fluid in the channel having an interface with the drive fluid plug in the channel; and

a magnetic drive for the drive fluid mounted exterior to the microchip, the magnetic drive being configured to form a changing magnetic field that in operation may drive driven fluid along the channel by changing the location of the interface between the drive fluid plug and the driven fluid.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,318,970 B1
DATED : November 20, 2001
INVENTOR(S) : C.J. Backhouse

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 7,
Line 19, "claim **1**" should read -- claim **2** --
Line 22, "claim **2**" should read -- claim **3** --

Column 8,
Line 2, "and covered" should read -- and is covered --

Signed and Sealed this

Fourteenth Day of May, 2002

Attest:

JAMES E. ROGAN
Director of the United States Patent and Trademark Office

Attesting Officer